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**Bidirectional relationships between vision and hearing loss with anxiety: prospective findings from the Three-City Study**

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*Running Head: Relationships between hearing and vision loss with anxiety*

**Objective:** To examine the bidirectional association between vision loss (VL) and hearing loss (HL) with anxiety over 12 years.

**Design:** Prospective population-based study.

**Setting:** Community dwelling French adults

**Participants:** 3928 adults aged 65 and above from the Three-City study.

**Measurements:** The relationships between vision loss, as assessed by near visual acuity, and self-reported hearing loss with Generalized Anxiety Disorder (GAD) diagnosis over 12 years were assessed. A further objective was to explore whether sensory loss has a differential relationship with GAD than with anxiety symptoms, assessed by the Spielberger's State-Trait Anxiety Inventory.

**Results:** At baseline, hearing loss (OR = 1.41, 95% CIs 1.02-1.96,  $p = 0.04$ ); but not mild or moderate to severe vision loss was associated with self-reported anxiety symptoms (OR=1.07 95% CIs 0.63-1.83,  $p = .80$ , OR = 0.66 95% CIs 0.12-2.22,  $p = 0.50$ ; respectively). Neither vision nor hearing loss was significantly associated with incident GAD. Baseline GAD was related to increased risk of incident HL (OR = 1.17, 95% CIs 1.07-1.28,  $p < .001$ ), but not mild or moderate to severe VL (OR = 1.01, 95% CIs 0.96-1.06,  $p = 0.81$ , OR = 0.97, 95% CIs 0.89-1.05,  $p = 0.45$ ).

**Conclusions:** Increased anxiety symptoms were observed in older adults with HL, whereas we found no evidence for an association between VL and anxiety. GAD was prospectively associated with increased risk of reporting hearing loss, possibly via sensory deprivation. Improved detection of

anxiety in older adults HL may improve quality of life and those with GAD may benefit from screening for HL.

**Key words:** anxiety disorders, generalized anxiety disorder, mental wellbeing, sensory impairment, older adults

**Key points:**

- Hearing loss in older adults is associated with increased anxiety symptoms
- We found no evidence of a longitudinal association between vision loss and anxiety
- A history of Generalized Anxiety Disorder increases risk of self-reporting new onset of Hearing Loss in older adults
- This study provides the first longitudinal examination of relationships between sensory loss and anxiety

Sensory losses are highly prevalent amongst older adults [1] and are amongst the top 10 contributors to burden of disease [2]. Older adults with sensory loss experience poorer mental health and reduced quality of life [3, 4]. An increased risk of depression in older adults with HL [5] and VL [6] has been established, with some evidence also suggesting that the prevalence of anxiety is higher than that for depression amongst older adults with VL [7, 8]. Indeed, prevalence of anxiety disorders in older adults is consistently reported to be higher than prevalence of depression [9, 10], and anxiety and depression are highly comorbid; with anxiety frequently preceding the onset of depression [11]. Yet there remains a dearth of research examining anxiety in sensory loss and older adults [4, 11]. Notably, in other chronic conditions, treatment of anxiety rather than depression has yielded better physical and psychological outcomes [12, 13], underscoring that unidentified and untreated anxiety might also underlie relationships between physical ill-health and mental wellbeing. Accordingly, a better understanding of anxiety disorders amongst older adults with sensory loss is needed.

Of the few anxiety and sensory loss studies to date, cross-sectional associations between anxiety with VL [8, 14, 15] have been reported; although findings remain equivocal [16, 17]. Limited cross-sectional studies also indicate an increased risk of anxiety in older adults with HL. However, longitudinal explorations of an association between sensory loss and anxiety are lacking. Further gaps in the anxiety and sensory loss literature remain. Most studies have examined anxiety symptoms; however less is known about anxiety disorders. To date, the anxiety measures utilised typically fail to distinguish between threshold and subthreshold anxiety, yet varied prevalence rates of threshold and subthreshold disorders in sensory losses have been observed [15]. Moreover the measures used assess a broad range of symptoms rather than assessing symptoms characteristic of any specific anxiety disorder. Thus, little is known about the extent to which relationships are limited to broad anxiety symptoms or are specific to (threshold) anxiety disorders. Generalized Anxiety Disorder (GAD), characterized by the hallmark feature of worry, is among the most prevalent anxiety disorders in older persons [18], and has a deleterious impact on quality of life [9]. Whether the diagnosis of GAD has a differential association with sensory loss compared with self-reported anxiety symptoms remains unclear.

Furthermore, especially in younger adults, those with sudden sensorineural hearing loss reported higher rates of having previously experienced an anxiety disorder than healthy controls [19] and adults with tinnitus retrospectively reported higher rates of worry (characteristic of GAD) than

controls [20]. In addition, anxiety has been shown to decrease the ability to manage hearing loss, leading to a worsening of the loss [21]. Despite these nascent findings, prospective explorations of an association between anxiety and incident sensory loss are lacking. Therefore this study aims to: a) examine the bi-directional longitudinal association of near VL and self-reported HL with GAD diagnosis; and b) explore whether sensory loss has a differential relationship with GAD diagnosis than self-reported anxiety symptoms.

## **Method**

This study forms part of the SENSE-Cog multi-phase research programme, funded by European Union Horizon 2020 programme. SENSE-Cog aims to promote mental well-being in older adults with sensory and cognitive impairments (<http://www.sense-cog.eu/>) [22].

### *Sample*

This paper examines data from the Three-City study [23], a prospective cohort study of 9294 community-dwelling French adults aged 65 years and above. Participants were recruited via the electoral roles of three French cities (Bordeaux, Dijon and Montpellier). The initial acceptance rate was 37%. Data from the Bordeaux and Montpellier sites are examined (N=4363), where baseline assessment for GAD was undertaken in 1999-2001. The Three-City study protocol was approved by the Ethical Committees of the University–Hospitals of Bicêtre and Nîmes (France) and written informed consent was obtained from participants. Participation included a face-to-face interview and clinical examinations. Participants were followed up at 2-3 year intervals for up to 12 years. Among the initial sample, 3953 (90.6%) have been followed-up at least one time over the 12-year period; 116 had died before the first follow-up and 1411 by the end of the 12-year period.

### *Anxiety Measures*

GAD diagnosis was ascertained by the Mini International Neuropsychiatric Interview (MINI) [24]. Both current and lifetime history of GAD, based on DSM-IV criteria, were assessed by trained

nurses or psychologists. The MINI was administered at baseline, as well as at 7, 10 and 12 years. (435 not assessed at baseline were excluded). Prevalent cases were those with a current diagnosis of GAD and, at each follow-up visit, incident cases were defined as those presenting with a new (and current) diagnosis among those free of GAD at baseline.

Self-report anxiety symptoms were measured at baseline only using the Spielberger's State-Trait Anxiety Inventory (STAI); a well validated and reliable measure of anxiety symptomatology [25]. Form Y was used to assess trait anxiety symptomatology, assessed by 20 questions rated on a four-point Likert scale. Scores range from 20-80 with higher scores indicative of greater symptom severity. Although varying cut-off scores have been proposed, a cut-off of 54 has been shown to have good sensitivity in older adults [26]. The STAI was administered as part of a self-completed questionnaire. Only participants who completed the STAI (n=2934) were included in anxiety symptom analyses.

#### *Sensory Loss Measures*

Sensory loss was assessed at each follow-up. Binocular near visual acuity (presenting vision) was assessed using the Parinaud scale with a standardized reading distance of 33 cm. Mild VL was classified as Parinaud 3 or 4 (Snellen equivalent 20/30-20/60) and moderate to severe VL as Parinaud > 4 (Snellen equivalent < 20/60). Hearing loss was based on one question with 4 response categories and was classified as self-reported deafness or difficulty understanding a conversation.

#### *Socio-demographic and health variables*

Socio-demographic and health-related information was collected during the standardized interview; including education (elementary, secondary school, higher education), monthly income (<€760, €760-2280, >€2280), marital status, alcohol consumption (<10, 10-40, >40 grams per day), tobacco use (current-, past -, or non-smoker), and falls in the past year. A composite score representing functional ability was also calculated based on the Rosow-Breslau scale, Lawton-Brody Brody Instrumental Activities of Daily living (IADL) scale and the Katz Index of Independence in Activities of Daily Living (categorized as autonomous; mobility limitations; mobility and IADL

limitations; and limitations in three or more areas) [27]. During the medical questionnaire, history of stroke, myocardial infarction, depression diagnosis (MINI), diabetes, and use of psychotropic medication (ATC codes: N05A-C, N06A-B) was obtained. A medical examination assessed Body Mass Index (BMI) ( $\leq 25$ ,  $>25$ ), and blood pressure was measured using a digital electronic tensiometer OMRON M4. Hypertension was defined as 140/90 mmHg or treatment with blood-pressure lowering drugs. Cognitive functioning was assessed using the Mini-Mental State Examination (MMSE;  $<16$ ,  $16-23$ ,  $\geq 24$ ).

### *Statistical Analysis*

Socio-demographic and health characteristics were compared by sensory loss using chi-squares and one-way ANOVAs. Logistic mixed models [28] were used to explore the bi-directional relationships between sensory loss and GAD. Logistic mixed models are optimal for exploring reversible binary outcomes given that they take into account within-subject correlation and model the individual time evolutions of the outcome (incident GAD or incident sensory loss) across follow-up, thus allowing for reversibility of symptoms. Mixed models also allow for greater flexibility to model time effects and handle missing data. In participants free of GAD at baseline, we examined whether baseline VL or HL was associated with incident GAD. We systematically searched for potential interactions between vision and hearing and sensory loss with sex and education. Logistic mixed models were also undertaken to explore the effect of baseline anxiety on incident HL in those free of HL at baseline, and on incident VL in those free of VL at baseline. Additional models tested if a lifetime history of GAD prior to baseline predicted subsequent VL or HL. To examine if there is a cross-sectional relationship between anxiety symptoms and GAD with sensory loss, logistic regression analyses assessed if baseline VL or HL was associated with baseline presence of anxiety symptoms or GAD.

For each analysis, three models were undertaken; Model 1 adjusted for time (longitudinal analyses only), sex, study center, and age; Model 2 also adjusted for education, income, marital status, and use of psychotropic medication; and Model 3 further adjusted for MMSE, functional ability, falls, BMI, hypertension, diabetes, smoking, alcohol, depression, and history of stroke and myocardial infarction. Analyses were conducted using SAS 9.4 (SAS Institute, Inc., Cary, NC).

## Results

Of the eligible 3921 participants, mean age at baseline was 73.7 (SD = 5.2) and the majority was female (n=2343; 59.8%). Baseline prevalence of mild VL was 11.7% (n=460), moderate to severe VL was 2.6% (n=104), and 36.1% (n=1419) for HL. Those with sensory loss were older than those with no loss and in poorer health on all the health characteristics examined (see Appendix 1). Those with VL were also less educated and had lower incomes. At baseline, 97 (2.5%) participants met criteria for a current GAD, with total 220 reporting a lifetime history of GAD. Those with and without a GAD history had few demographic differences, although participants with GAD were more likely to be female (70.9% vs 50.1%,  $p < .001$ ) and were more highly educated ( $p < .001$ ).

### *Sensory loss and anxiety: cross-sectional analysis*

At baseline, VL was not associated with anxiety symptoms (Table 1). HL, however, was significantly associated with anxiety symptoms (OR = 1.41, 95% CIs 1.02-1.96,  $p = 0.04$ ). Neither VL nor HL had significant cross-sectional associations with current GAD.

### *Sensory loss and anxiety: longitudinal analysis*

Of the 3824 participants without current GAD at baseline, incident GAD was detected in 82 individuals over follow up. Neither mild nor moderate to severe VL (OR = 0.73, 95% CIs 0.22-2.43,  $p = 0.60$ ; OR = 0.77, 95% CIs 0.12-4.86,  $p = 0.78$ ; respectively) predicted GAD onset (Table 2). HL was also unrelated to GAD onset (OR = 1.13, 95% CIs 0.59-2.17,  $p = 0.71$ ).

### *Anxiety and sensory loss onset*

Onset of any VL was noted in 1122 participants without VL at baseline. Neither current nor lifetime history of GAD was associated with incident VL (Table 3). In those free of HL at baseline, 1256 participants reported HL onset during follow-up. Both a current diagnosis of GAD and a lifetime history



of GAD was associated with self-reported HL onset (OR = 1.17, 95% CIs 1.07-1.28,  $p < .001$ ; OR = 1.07, 95% CIs 1.01-1.13,  $p = 0.02$ ; respectively). Baseline anxiety symptoms were not associated with incident sensory loss. All tested interactions were non-significant.

## Discussion

To our knowledge this study provides the first longitudinal examination of the bi-directional association between anxiety and sensory loss. HL was associated with self-reported anxiety symptoms, but not prevalent or incident GAD, while VL was not associated with anxiety. Both a current diagnosis and a lifetime history of GAD was associated with increased likelihood of reporting HL over 12 years.

Consistent with the limited literature, HL was associated with increased anxiety symptomatology [29, 30]. Vision, was not found to be related to anxiety, nor was the VL and HL interaction significant; concordant with previous results that anxiety is more common in HL than VL [17]. An association with HL but not an interaction with VL suggests that anxiety in HL may be due to social isolation and communication difficulties [29]. No observed association between VL and anxiety in our data builds on the currently equivocal literature [14-16]. The heterogeneity of anxiety measures used might explain the conflicting results. Different symptoms of anxiety, often reflecting different underlying anxiety disorders, are examined across the anxiety measures used. Agoraphobia and social phobia are reported to be the most prevalent anxiety disorders amongst older adults with VL [15], thus vision may be associated only with specific symptoms or anxiety disorders that were not assessed in our study.

Although a relationship between HL and anxiety symptoms was observed, neither VL nor HL was associated with current or incident GAD. Due to the self-reported assessment of HL in our study, an inverse causation cannot be excluded to explain our results, however, our finding that HL was associated with increased symptoms but not GAD diagnosis may be a reflection of older adults frequently having elevated, yet subthreshold, mental health symptoms [11, 15]. This may be due, at least partially, to the difficulty in diagnosing anxiety disorders in later life; including in research settings

[11]. Anxiety in older age can manifest differently than in younger adults and, additionally, symptoms such as avoidance and excessive worry can be perceived to be normative parts of ageing [11]. Alternatively, the association of HL with increased anxiety symptoms, but a non-significant association with GAD, might be explained by the symptoms examined. The STAI assesses a range of affective and physiological anxiety symptoms, not only those specific to GAD. It is possible that HL is more closely related to other anxiety disorders. Especially given the communication limitations, specific situations such as social interactions and going out alone may be more anxiety-provoking; thus social phobia and agoraphobia might be more common in HL. The contrasting anxiety and sensory loss findings to date, as well as the differential relationship between HL with anxiety symptoms and GAD, further underscore the need for ongoing disorder-specific research in sensory loss. Disorder specific examinations will provide a clearer picture of the mental health needs of older adults with sensory loss, and will enable better comparison across studies.

Notably, although sensory loss was not associated with GAD onset, we found that both a current diagnosis and a lifetime history of GAD was associated with a small but significant increased risk of reporting HL. Adults with sudden sensorineural HL have a greater history of anxiety disorders than controls, although the relationship decreased with age [19]. Similarly, adults with sudden onset HL or tinnitus retrospectively reported higher rates of worry – a central feature of GAD – than controls, although this was no longer significant after adjustment [20]. Our findings suggest that links between anxiety and worry with hearing are not limited to sudden hearing loss and that, amongst older adults, there is a prospective relationship between GAD and HL.

The observed relationship between GAD and incident HL could be explained by several mechanisms. Cardiovascular risk factors are frequently associated with GAD [31], as well as HL in older adults [32]. Another pathway is through inflammatory processes or impaired hypothalamic–pituitary–adrenal axis function. GAD is associated with elevated inflammatory markers [33] and inflammatory markers are also involved in the pathogenesis of HL [19]. It has also been proposed that increased hypothalamic–pituitary–adrenal (HPA) axis activity observed in GAD might impact hearing [15]. Unhealthy lifestyle and behavioural factors also possibly underlie this relationship. Additionally, social restriction and avoidance are common in anxiety, which may impact hearing via sensory deprivation [29]. Alternatively, anxious people might be more likely to self-report HL over time.

The relationships between anxiety and HL further highlight the importance of identifying and treating anxiety in older adults; elevated symptoms that remain subclinical cause substantial distress [34]. However, older adults with anxiety underutilise mental health services [9, 18] and are rarely diagnosed [11]. Thus targeted interventions would be beneficial. Communication skills training has reduced psychological distress in older adults with HL [35]. Internet-based therapies for the treatment of psychological distress in older adults, especially those with HL might also be a valuable avenue [36].

### *Strengths and Limitations*

This study substantially contributes to the dearth of literature examining anxiety in older adults with sensory loss. Strengths include the large sample, length of follow up and the exploration of both VL and HL, as well as an anxiety diagnosis in addition to self-report symptoms. Limitations include that hearing loss was self-reported, using a single item. Such self-reports may represent underestimates of actual HL, due to perceptions that hearing decline is a natural part of aging. Conversely, those who have anxiety might be more likely to self-report HL onset, although self-reported vision did not have a relationship with anxiety (see appendix 2). Ongoing research with objective assessments of hearing loss would be invaluable to corroborate such associations. A further limitation of this study was that the STAI was administered only at baseline, thus the long-term trajectory of anxiety symptoms could not be examined. Longitudinal differences between anxiety symptoms and GAD diagnosis remain unexplored. Only GAD was assessed, if there are relationships between other anxiety disorders with sensory loss should be examined in future. Furthermore, incident GAD was assessed only during follow-up interviews, thus remitted cases of GAD were not included in incident analyses. Power was low for the analysis of incident GAD, especially in VL, thus precluding definitive conclusions. Whilst our findings highlight the presence of an association between anxiety and sensory loss, we cannot determine causality because of the longitudinal cohort design and infrequent measures of VL, HL and GAD.

### *Conclusions*

HL was significantly associated with anxiety. Older adults with HL were more likely to have elevated anxiety symptoms, although were not at increased risk of GAD. Other anxiety disorders are likely to be more prevalent in older adults with sensory loss. In addition, GAD was prospectively associated with self-reporting the onset of HL. Better detection of anxiety in older adults with HL may improve their quality of life and, concomitantly, ageing adults with a history of GAD may benefit from screening for hearing loss.

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**Table 1: Cross-sectional association between baseline type of sensory loss (predictor variables) with anxiety symptoms (STAI) and GAD diagnosis (outcome variables). Three-City Study 1999-2001.**

	Model 1			Model 2			Model 3			
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p	
<b>Self-report anxiety symptoms</b>										
Mild vision loss	1.26	0.82 1.93	.30	1.09	0.68 1.75	.72	1.07	0.63 1.83	.80	
Moderate to severe vision loss	1.37	0.67 2.83	.39	1.49	0.68 3.26	.32	0.66	0.12 2.22	.50	
Hearing loss	1.61	1.23 2.10	.001	1.57	1.19 2.07	.002	1.41	1.02 1.96	.04	
<b>GAD diagnosis (current)</b>										
Mild vision loss	1.34	0.64 2.81	.44	1.33	0.63 2.80	.46	1.49	0.69 3.20	.31	
Moderate to severe vision loss	0.29	0.02 4.75	.39	0.29	0.02 4.57	.38	0.30	0.02 4.60	.39	
Hearing loss	1.30	0.85 2.00	.23	1.31	0.85 2.00	.23	1.08	0.68 1.71	.76	

OR: odds ratio

CI: confidence interval

Model 1: STAI n=2934 GAD n=3892; adjusted for sex, age, center

Model 2: STAI n=2800 GAD n=3695; adjusted for sex, age, center, education, income, marital status, psychotropic medication use

Model 3: STAI n=2540 GAD n=3328; adjusted for sex, age, center, education, income, marital status, psychotropic medication use, MMSE, functional ability, falls, BMI, hypertension, diabetes, smoking, alcohol consumption, depression, and history of stroke and myocardial infarction



**Table 2: Baseline type of Sensory Loss (predictor variables) and incident GAD (outcome variable) over 12 years**

	Model 1			Model 2			Model 3		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
<b>Incident GAD</b>									
Mild vision loss	0.67	0.20 2.20	.51	0.65	0.20 2.15	.48	0.73	0.22 2.43	.60
Moderate to severe vision loss	1.24	0.29 5.30	.78	1.17	0.27 5.04	.84	0.77	0.12 4.86	.78
Hearing loss	1.32	0.72 2.42	.36	1.31	0.71 2.39	.39	1.13	0.59 2.17	.71

Model 1: n=3798; adjusted for time, sex, age, center

Model 2: n=3604; adjusted for time, sex, age, center, education, income, marital status, psychotropic medication use

Model 3: n=3242; adjusted for time, sex, age, center, education, income, marital status, psychotropic medication use, MMSE, functional ability, falls, BMI, hypertension, diabetes, smoking, alcohol consumption, depression, and history of stroke and myocardial infarction

**Table 3: Anxiety (predictor variables) and incident Sensory Loss (outcome variables) over 12 years**

	OR	95% CI	P
<b>Mild Vision Loss</b>			
<i>Current GAD</i>			
Model 1	1.02	0.97 1.07	.38
Model 2	1.01	0.97 1.06	.58
Model 3	1.01	0.96 1.06	.81
<i>Lifetime GAD</i>			
Model 1	1.00	0.97 1.04	.89
Model 2	1.00	0.97 1.03	.93
Model 3	0.99	0.96 1.03	.66
<i>Self-report anxiety symptoms</i>			
Model 1	1.26	0.99 1.65	.10
Model 2	1.18	0.89 1.56	.25
Model 3	1.05	0.74 1.47	.80
<b>Moderate to Severe Vision Loss</b>			
<i>Current GAD</i>			
Model 1	0.97	0.90 1.05	.51
Model 2	0.97	0.90 1.05	.49
Model 3	0.97	0.89 1.05	.45
<i>Lifetime GAD</i>			
Model 1	1.00	0.95 1.06	.88
Model 2	1.00	0.95 1.05	.91
Model 3	1.00	0.95 1.06	.96
<i>Self-report anxiety symptoms</i>			
Model 1	0.98	0.59 1.64	.95
Model 2	1.03	0.61 1.74	.92
Model 3	1.03	0.55 1.91	.93
<b>Hearing loss</b>			
<i>Current GAD</i>			
Model 1	1.16	1.07 1.25	.001
Model 2	1.17	1.08 1.27	<.001
Model 3	1.17	1.07 1.28	<.001
<i>Lifetime GAD</i>			
Model 1	1.07	1.02 1.13	.01
Model 2	1.07	1.02 1.13	.01
Model 3	1.07	1.01 1.13	.02
<i>Self-report anxiety symptoms</i>			
Model 1	1.23	0.75 1.69	.56
Model 2	1.18	0.78 1.79	.43
Model 3	1.30	0.81 2.11	.28

Model 1: VL and GAD n= 2988, VL and STAI n= 2433, HL and GAD n=2299, HL and STAI n= 1707; adjusted for time, sex, age, center

Model 2: VL and GAD n= 2864, VL and STAI n= 2353, HL and GAD n=2192, HL and STAI n= 1651; adjusted for time, sex, age, center, education, income, marital status, psychotropic medication use

Model 3: VL and GAD n= 2610, VL and STAI n= 2159, HL and GAD n=1992, HL and STAI n= 1524; adjusted for time, sex, age, center, education, income, marital status, psychotropic medication use,

MMSE, functional ability, falls, BMI, hypertension, diabetes, smoking, alcohol consumption, depression, and history of stroke and myocardial infarction