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Is there a relation between sudden sensorineural hearing loss and white matter lesions?

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Abstract

Purpose Sudden sensorineural hearing loss (SSNHL) has similarities to conditions with vascular etiologies such as myocardial infarction and cerebral stroke. Thus, it could be considered as an early sign of a vascular disease and not only a specific local condition. Chronic hypoperfusion in the brain districts leads to a chronic ischemic damage, called cerebral small vessel disease (CSVD), detectable with brain magnetic resonance imaging (MRI).

Methods The authors used CSVD to establish the presence of vascular risk factors in individuals with SSNHL and used the Fazekas score scale to classify them.

Results Our study showed that individuals with SSNHL aged between 48 and 60 years have 26% more probability to have a Fazekas score higher than 1 compared to the general population. Individuals younger than 28 years showed a statistically significant negative correlation to have a Fazekas score higher than 0. The higher is the Fazekas score, the less is the probability of hearing recovery. The medium hearing-recovery probability is 46%. This decreases by 16% for every increase of score in the Fazekas scale. In the present study, the recovery probability decreased from 80% in individuals younger than 48 years with a score of 0 to 14% in individuals with a Fazekas scores of 3 and 4.

Conclusions The authors assessed a higher prevalence of CSVD compared to the general population in patients aged between 48 and 60 years with SSNHL. Moreover, they assessed that the presence of CSVD is related to a decreased probability of recovery, as it has already been demonstrated for stroke.

Keywords Sudden sensorineural hearing loss · Cerebral gliosis · Brain MRI · Vascular risk factors · Recover probability

Introduction

Sudden sensorineural hearing loss (SSNHL) is considered as a medical emergency [1] mainly affecting individuals between 50 and 60 years of age, although young healthy subjects could also be affected. Many causes of SSNHL have been suggested, but its pathogenic theories are multiple and controversial, including viral infection, vascular conditions, neoplasms, trauma, ototoxicity, autoimmune diseases, developmental anomalies and psychogenic disorders. A specific cause is identifiable in less than 5% of patients and an idiopathic origin is indicated in the majority of cases [2–9].

SSNHL has acute onset and unilateral symptoms, similar to the clinical picture of vascular events such as myocardial infarction, cerebral stroke and amaurosis fugax [10–15].

It is supposed that the SSNHL is not due to thrombotic events or vascular spams, but due to blood pressure dysregulation (BPD) of the stria vascularis [16, 17]. BPD, a process

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related to age, hypertension, diabetes [18], hypercholesterolemy and cigarette smoking [19–21], was first described in the cochlear–vestibular blood circulation by Fisch in 1972 [22]. It derives from the pathological alterations that follow cochlear atherosclerosis (CA), in which the tunica adventitia loses fibroblasts and becomes thicker because of the fibrous hyalinosis, while the number of the fibromuscular cells is reduced leading to decreased adrenergic regulations on the fibromuscular cells [23]. The reduction of the internal calibre of the cochlear–vestibular vessel and the BPD, which are typical of CA, may therefore, have a central role in SSNHL, especially following variations of the plasmatic viscosity, of the red blood cell deformation index and of the platelet aggregation, to which the stria vascularis is highly sensitive.

Cerebral small vessel disease (CSVD) is a term used for different pathological processes that affect the small vessels of the brain, such as small arteries, arterioles, capillaries and small veins. CSVD has a central role in central vascular events such as deep or cortical haemorrhages and lacunar cerebral infarction, and is associated to cognitive decline, dementia, depression and gait problems [24–27]. Several studies have indicated that CSVD can be preceded by white matter lesion (WML), areas of altered signal found in the white matter of the brain and visible as hyperintense spots on T2-weighted magnetic resonance imaging (MRI) and hypointense on computed tomography [28–30].

It is known that CSVD of the white matter shares pathophysiological aspects with the cochlear–vestibular system. The purpose of the present study is to evaluate if there is a correlation between CA of the cochlear–vestibular system and CSVD using brain MRI in patients with SSNHL.

Materials and methods

Selection of patients

One-hundred thirteen patients with a clinical diagnosis of idiopathic SSNHL (ICD-10: H912) were admitted to our University Hospital from January 2013 to December 2017 (study group), and 107 case–control subjects with similar demographic characteristics were included in this retrospective case–control study. SSNHL was defined as a sensorineural hearing loss greater than 30 dB over three contiguous pure-tone frequencies occurring within a 3-day period. Patients with previous cerebrovascular disease were excluded.

Patients were studied with pure tone audiometry (PTA) at admission and after 3 and 6 months from the SSNHL episode. All the patients were treated with intramuscular steroids, as previously described [31].

All the patients in the study and control groups underwent a brain MRI with contrast agent. To demonstrate the subcortical and periventricular gliotic lesions, T2 FLAIR sequences were evaluated, and subcortical and periventricular lesions were classified through the Fazekas scale [32], with a score from 0 (no lesions) to 6. On the basis of the MRI findings, patients were subdivided into five subgroups: I: score = 0; II: score = 1; III: score = 2; IV: score = 3; V: score = 4 or more. There were no patients with a score of 5 or 6.

Statistical analysis

Statistical analysis was performed using Prism GraphPad v7. Descriptive statistics, mean and standard deviation were calculated for numeric variables; frequency and percentages were calculated for categorical variables. A binary variable equal to 1 for Fazekas score higher than 0 (dummy score) was considered.

A regression model with three different specifications was used to evaluate the relationship between SSNHL and Fazekas score. The prediction of a "linear probability model", where the "dummy score" is the dependent variable, was reported in the model m1. Moreover, a number of dummy variables were introduced in the regressors. The first four dummy variables are the result of the interaction between the variable "Hearing Loss" and the age (hypo_under28, hypo_28-47, hypo_48-60 and hypo_over60). The control variables female (1 for female patients) and weight (Kg) were added. To avoid bias, the outliers were excluded (age and weight above the 99 percentile and the little number of individuals with Fazekas scores higher than 3).

A linear regression model (m4) with the variables hearing recovery, Fazekas score, weight and sex was used to evaluate the relationship between Fazekas score and hearing recovery. The model m5 shows a logistical valuation. The related variables weight and sex (female) were entered (m6). A logistic prediction on the effect of the Fazekas score on the hearing-recovery possibility was calculated with the non-linear model m5.

The p value for assessing statistical significance was an α of 0.05.

Results

Patients' characteristics

Two-hundred twenty patients were included in the study; 113 patients in the study group and 107 in the control group. In the study group, 70 were females and 43 were males. The mean age was 44 years (17–73 years). Mean weight was 64 kg (50–92 kg). All the subjects were white, and no woman was pregnant.

Table 1 XXXX

Description	Fazekas score	Dummy score	Age	Female	Weight
Mean	0.77	0.42	44.54	0.62	64.79
SD	1.08	0.50	17.33	0.49	12.60
P10	0.00	0.00	17.00	0.00	50.00
P99	4.00	1.00	73.00	1.00	92.00

Descriptive characteristics of the sample of 113 individuals included in the study group

P10: tenth percentile; P99: ninth percentile; dummy score: binary variable equal to 1 for Fazekas score higher than 0; weight in kilograms

Table 2 XXXX

Fazekas score	0	1	Total
0	58.33	58.82	58.56
1	18.33	17.65	18.02
2	10.00	17.65	13.51
3	11.67	3.92	8.11
4	1.67	1.96	1.80
Total	100.00	100.00	100.00

The incidence of the gliotic lesions, classified through the Fazekas scale, is compared between the patients with a diagnosis of SSNHL (1) and the control group (0). In the analysis, the authors considered the grades from 0 to 4 of the Fazekas scale (0–4)

Table 1 shows the characteristics of Fazekas score, age, sex and weight of individuals in the study group. The mean of the variable "Score" was 0.77, meaning that most of the subjects (58%) belong to the lowest class of the Fazekas score (0). The population with the maximum score of 4 is out of the 99 percentiles. Forty-two individuals reported a "dummy score" higher than 1 for Fazekas score higher than 0. This value was used in the regression analysis to evaluate the relationship between a positive Fazekas score and SSNHL.

Table 2 compares the incidence of the gliotic lesions, classified through the Fazekas Scale, in patients in the study and control groups. Nearly 90% of the individuals in both groups had a Fazekas score lower than 3, and 8.11% had a Fazekas score of 3, mainly in the control group (77%). Only two individuals had a Fazekas score of 4. The majority of patients under 28 years in both groups had a Fazekas score of 0 and only two of them had a score of 1.

Table 3 shows individual characteristics of subjects in both groups. No significant differences were noted for dummy score, sex and age. Patients in the study group had a mean weight of 5 kg higher than the control group.

Table 3 XXXX

SSNHL diagnosis	Fazekas score	Dummy score	Age	Female	Weight
0	0.80	0.43	44.75	0.62	62.19
1	0.73	0.42	44.29	0.62	67.75
Mean	0.77	0.42	44.54	0.62	64.79

Comparison of the study and control groups to evaluate individual characteristics

0, SSNHL diagnosis; 1, control group; dummy score, a binary variable equal to 1 for Fazekas score higher than 0; age, years old; female, ratio female/male; weight in kilograms

Table 4 XXXX

Age-related groups	m1 (b/p)	m2 (b/p)	m3 (b/p)
Hypo_under28	− 0.239 (0.09)	− 0.242 (0.08)	
Hypo_28-47	0.215 (0.18)	0.232 (0.13)	0.191 (0.24)
Hypo_48-60	0.262 (0.07)	0.258 (0.07)	0.271 (0.06)
Hypo_over_60	− 0.051 (0.80)	− 0.028 (0.88)	0.009 (0.96)
Female	0.102 (0.44)		0.139 (0.31)
Weight	0.001 (0.84)		0.001 (0.83)
Constant	0.186 (0.64)	0.314 (0.00)	0.174 (0.67)

Relationship between hearing loss and Fazekas score. Regression model with three different specifications. The "dummy score" is the dependent variable and it is reported in the model m1. A number of dummy variables were introduced in the regressors. The first four dummies are the result of the interaction between the variable "Hearing Loss" with age-related dummy variables: hypo_under28, hypo_28-47, hypo_48-60 and hypo_over60. The control variables Female (1 for female patients) and Weight (in Kilograms) were added. m1, model 1; m2, model 2; m3, model 3

Relationship between Fazekas score and SSNHL

The relationship between Fazekas score and SSNHL was studied using a regression model with three different specifications (Table 4). The only significant results were related to the variables hypo_under28 and hypo_48–60. This indicates that individuals between 48 and 60 years with SSNHL have 26% more probability to have a Fazekas score higher than 1. For individuals under 28 years, the probability is instead negative, being just one patient diagnosed with SSNHL and a Fazekas score higher than 1. The coefficients estimate that SSNHL is not influenced by the control variables female and weight (model m2).

Relationship between Fazekas score and hearing recovery

PTA thresholds in the range 125–8000 Hz before and 6 months after treatment are shown in Fig. 1. Data are sorted by patients' Fazekas scores (Fazekas score = 0: PTA pre 65.7 dB, PTA post: 41.85 dB; Fazekas score = 1: PTA pre 68.1 dB, PTA post: 50.57 dB; Fazekas score = 2: PTA pre 74.57 dB, PTA post: 61.82 dB; Fazekas score = 3, 4: PTA pre: 88.57 dB, PTA post: 80.5 dB).

The mean recovery probability is 46%. A negative marginal and significant effect (16%) is associated to the Fazekas score, meaning that for every increase of score in the Fazekas scale, the probability to have a hearing recovery decreases by 16%. The recovery probability for Fazekas 0 was 71%, 55% for Fazekas 1, 39% for Fazekas 2 and less than 15% for Fazekas scores of 3 and 4 (Table 5).

In Table 6, the score was subdivided into three classes: score 0 is used, together with the age classes inferior to 48 years old, as a benchmark; the scores 1 and 2 ("mild" Fazekas) and scores 3 and 4 ("middle-severe" Fazekas) were called, respectively, sc_cl2 and sc_cl3. The two different regressions always showed negative and significant

Table 5 XXXX

	m4 (b/p)	m5 (b/p)	m6 (b/p)
Fazekas score	− 0.142 (0.04)	− 0.652 (0.05)	− 0.147 (0.04)
Female			− 0.018 (0.92)
Weight			0.003 (0.64)
Constant	0.574 (0.00)	0.319 (0.37)	0.361 (0.53)

Relation between Fazekas score and hearing recovery. Linear regression model m4 to study the relation between hearing recover (1 when achieved) and Fazekas score. The related variables Weight (in kilograms) and Sex (female) were entered (m6). A logistic prediction on the effect of the Fazekas score on the hearing recover possibility was calculated with the non-linear model m5. m4, model 4; m5, model 5; m6, model 6; b/p, regression coefficients and p values for each covariate

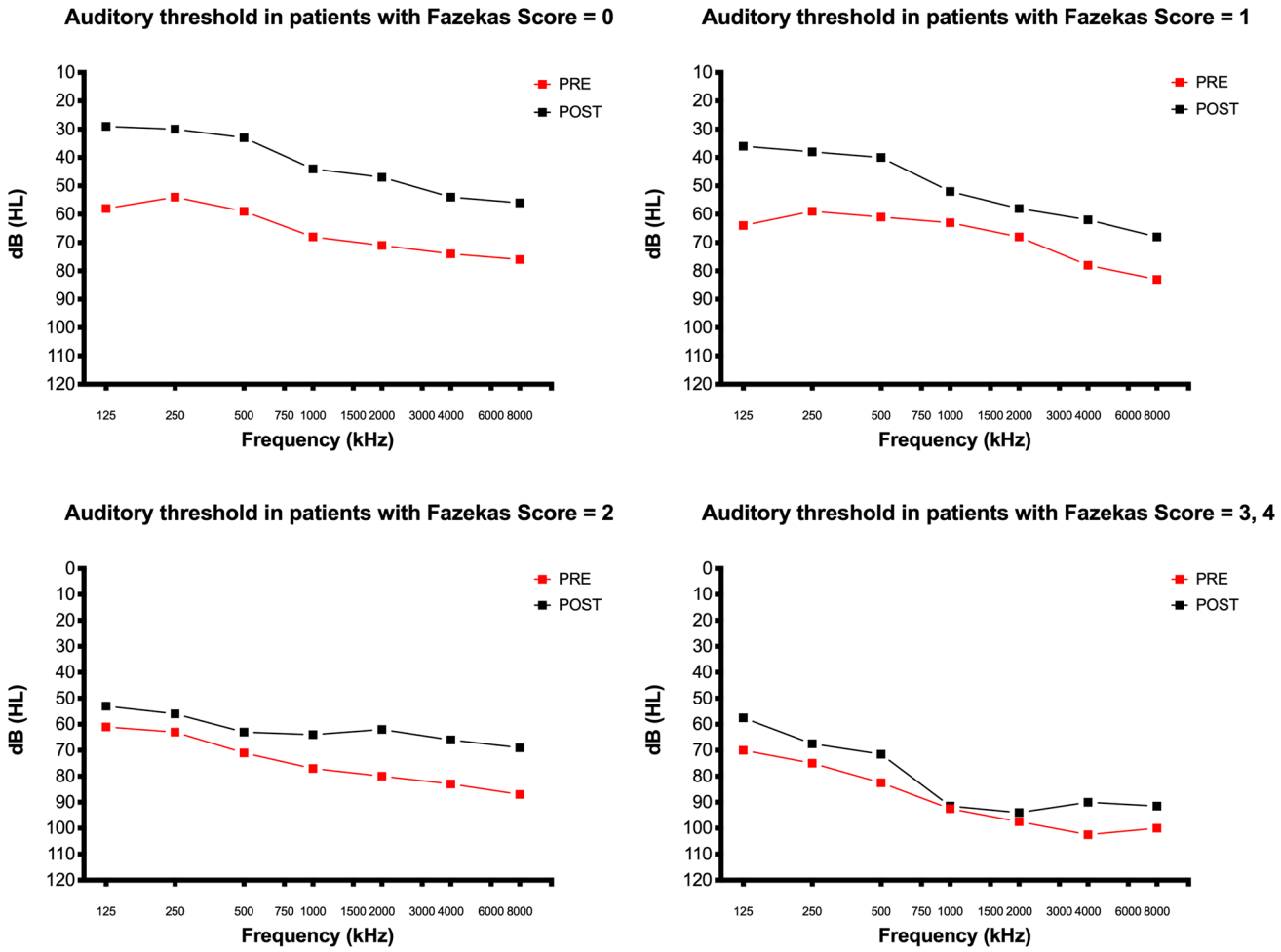

Fig. 1 XXXX

Table 6 XXXX

	m7 (b/p)	m8 (b/p)
sc_cl2	− 0.180 (0.26)	− 0.173 (0.29)
sc_cl3	− 0.657 (0.04)	− 0.660 (0.05)
48–60 years old	0.182 (0.29)	0.171 (0.33)
Over 60 years old	0.137 (0.51)	0.183 (0.44)
Female		− 0.146 (0.55)
Weight		− 0.003 (0.72)
Constant	0.491 (0.00)	0.804 (0.29)

Regression analysis: relation between hearing recovery and Fazekas score. With the linear regression model m7 and m8, the Fazekas score was subdivided into three classes: score 0 is used, together with the age classes inferior to 48 years old, as a benchmark, the scores 1 and 2 (mild Fazekas) and scores 3 and 4 (middle-severe Fazekas) were called, respectively, sc_cl2 and sc_cl3. The two different regressions show always negative and significant coefficients related to the scores 3 and 4. The recovery probability decreases from 80% for an individual younger than 47 years old with a score of 0 to 14% for an individual with scores 3 and 4 (model m8). m7, model 7; m8, model 8; m6, model 6

coefficients related to the scores 3 and 4. It is possible to calculate that the recovery probability decreases from 80% for an individual younger than 48 years with a score of 0 to 14% for an older individual with scores 3 and 4 (model m8). The relation between Fazekas score and probability of hearing recovery is statistically significant.

Discussion

In this case–control study, the authors aimed to evaluate if there was a correlation between CA and CSVD in patients with SSNHL using brain MRI.

Following hypoperfusion of the cochlea due to atherosclerosis, the number of inner and outer hair cells is progressively reduced, mostly at the basal turn, and a stiffening of the basilar membrane may be present [33]. This pathophysiological condition, in conjunction with the increase of the plasma viscosity, can lead to a suffering of the stria vascularis, without necessary leading to an acute cochlea ischemia [10, 34].

It is known that CSVD is present in 68–87% of the general population between 60 and 70 years, in 95–100% over 75 years old and in only 22% of the population younger than 40 years [35, 36]. In our study, 58% of the patients affected by SSNHL had a Fazekas score of 0. Particularly, 20 patients (17.5%) were younger than 28 years and just 1 of them had a Fazekas score > 0. It is, therefore, unlikely that the cause of SSNHL for younger individuals was CA. A Fazekas score of 3 or 4 was found in only 10% of the patients with SSNHL. The low mean age (44 years) of the recruited population could explain this finding. In fact, only 25 patients (22%) were enlisted in the subgroup of patients older than 60 years.

To date, several authors studied the relationship between CSVD, cerebral stroke and recovery from stroke [37], showing a decreased probability of neurological recovery after a stroke in patients with a middle-severe CSVD. These individuals also showed a higher risk of cerebral stroke recurrence. A recent study by Ciorba et al. investigated the presence of WMLs in subjects affected by SSNHL and the significance of WMLs in SSNHL patients. The authors reported that although the incidence of WMLs in patients with SSNHL was not different compared to that of the control group, MRI could have a prognostic role for SSNHL patients, as the presence of WMLs can been linked to a poorer hearing recovery rate [28].

The chronic ischemia induces the expression of an endothelial growth factor, leading to the constitution of a collateral leptomeningeal circulation [38, 39]. Thus, individuals with mild CSVD should have a better collateral circulation [40]. It is nevertheless important to notice that the collateral circulation was found even in patients with severe carotid stenosis and severe CSVD [41], and that the revascularization of the cerebral ischemic areas is not only due to the recanalization of the carotid arteries, but also due to the present collateral perilesional circulation [42]. The relation between SSNHL and Fazekas score showed a statistical significance only for the two variables hypo_under28 (0.09) and hypo_48-60 (0.07). Individuals in the study group aged between 48 and 60 years had 26% more possibility to have a Fazekas score higher than 1, and therefore, a CSVD when compared with the control group.

Lin et al. in 2008 demonstrated a higher risk of cerebrovascular disease in 5 years following the SSNHL episode, and since then, many other authors confirmed this finding [3, 15, 43]. In the present study, individuals with SSNHL showed a more advanced CSVD and a younger age (48–60 years) compared to the control group, suggesting a higher risk of cerebrovascular disease. On the contrary, individuals suffering from SSNHL under 28 years had a probability near 0 to have CSVD.

The analysis of the relationship between SSNHL, Fazekas score and hearing recovery denotes that the higher the Fazekas score is, the less probable is the hearing recovery. It was estimated a mean probability of recovery of 46%, with a decrease of 16% for every 1-point increase of Fazekas score.

When the authors consider three CSVD classes (0 for no CSVD, scores 1 and 2 for mild CSVD, scores 3 and 4 for middle-severe CSVD), and correlate these with the age-related classes, the probability decreases from 80% for an individual younger than 48 years with a score of 0, to less than 14% for individuals with scores 3 and 4, demonstrating a negative relationship between Fazekas score and hearing recovery.

Twenty-nine percent of the patients with a mild CSVD showed a hearing recovery; thus, it is possible to suppose that a reversible hypoxia or a neovascularization of the cochlea occurred, in contrast to the individuals showing a middle-severe CSVD (only 14% recovered).

Finally, it is nevertheless remarkable that the CA is a progressive disease, influenced from several risk factors, and that the Fazekas score could even reflect a different pathogenesis, which could then influence the prognosis.

Conclusions

In the present retrospective case–control study, we examined the relation between CA and CSVD in patients with SSNHL. Younger individuals showed no correlation with CSVD, therefore, in these patients, other causes for the SSNHL episode should be supposed. Individuals aged between 48 and 60 years showed a more advanced CSVD compared to the control group, suggesting a vascular origin of SSNHL. The relationship between SSNHL, Fazekas score and hearing recovery showed that the higher is the Fazekas score, the less is the probability to recover; this is similar to the evidence that the higher is the CSVD in patients who had a stroke, the less is the probability of a neurological recovery.

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Compliance with ethical standards

Conflict of interest All the authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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