Speech-in-noise as a biomarker of peripheral auditory neuropathy in metabolic disorders: proof of concept in patients with uncontrolled type 2 diabetes

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MAKING HEARING A PRIORITY

BACKGROUND

While retinopathy, nephropathy and peripheral neuropathy are among the well-established complications of type 2 diabetes, sensorineural hearing loss is not yet considered a comorbidity factor in diabetes.

However, according to some studies, **60% of patients with type 2 diabetes**, aged between 30 and 60, **have hearing loss**, and **50% of them have moderate to severe hearing loss** [1-3]. Several causes have been proposed to explain this silent epidemic, including cochlear microangiopathy, chronic systemic inflammation, and peripheral auditory neuropathy (synaptopathy), which lead to early sensorineural hearing loss [4].

Thus, nearly 200 million people with diabetes are estimated to have moderate to severe hearing loss for which no therapeutic solution exists other than the use of hearing aids. However, while these hearing aids partially improve audibility, they do not prevent the progression of hearing loss throughout the course of diabetes, nor do they improve speech intelligibility in noisy environments for these patients. Therefore, it is important to better characterize hearing pathology in diabetic patients.

METHODS

To better characterize this complication, we conducted a **clinical study on 349 participants** (42.3% men/57.7% women) under 70 years of age with moderately controlled type 2 diabetes (T2D) (HbA1c > 7%) for at least 2 years (Figure 1).

Participants were primarily (85%) recruited from the diabetology department at the Institute of Diabetology and Nutrition of the Centre (IDNC, Mainvilliers), with some additional inclusions from outpatient consultations and/or hospitalizations at the Carémeau University Hospital (Nîmes) and the Diabetic Foot Clinic (Grau-du-Roi).

A **comprehensive hearing test battery** was offered to participants, including otoscopy, tympanometry, otoacoustic emissions (DPOAE), complete audiometry (pure-tone air and bone conduction, speech in silence and in noise), and an electrophysiology session with auditory brainstem response (ABR) and electrocochleography (EcochG) recordings. (Figure 1)

The assessment also included the Montreal Cognitive Assessment (MoCA) as **cognitive screening test.**

The aim of the study being to explore forms of sensorineural hearing loss related to diabetes, 99 participants were excluded from the analysis because they primarily presented with abnormal otoscopy (n=16), abnormal tympanometry (n=6), conductive hearing loss (n=23), asymmetric hearing loss (n=6), or any combination thereof, thus having no apparent link to their diabetes. Furthermore, 9 participants could not complete the full battery of tests, resulting in a **final study size of 241 participants**. (Figure 2)

Figure 1. Study scheme and inclusion/exclusion criteria.

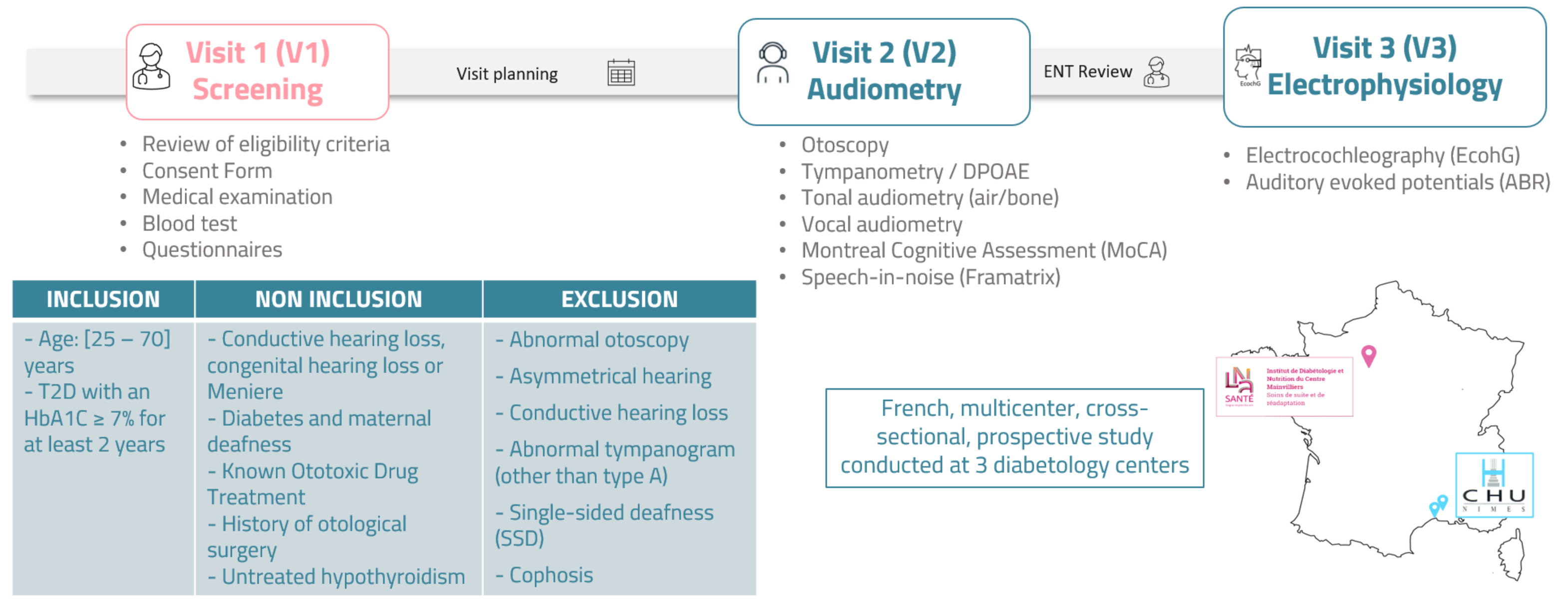


Figure 2. Study metrics.

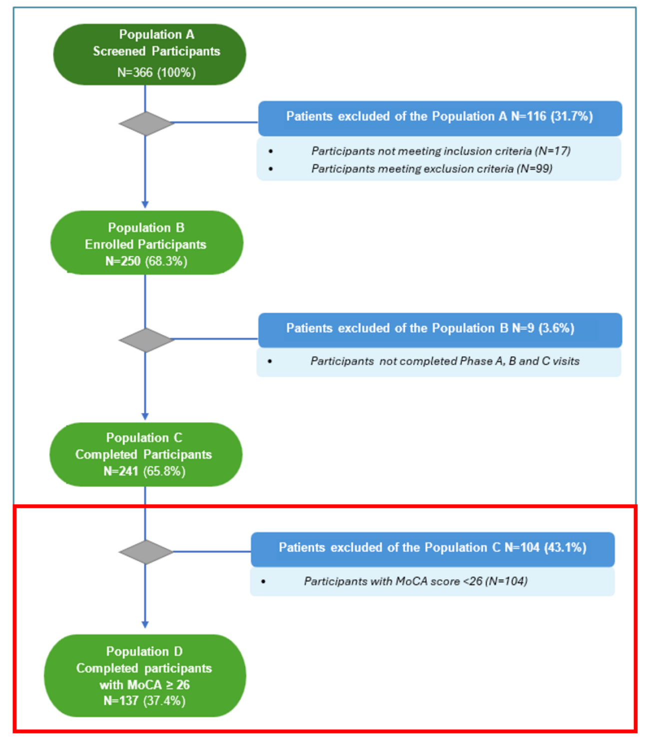


Table 1. Study population characteristics.

		All n = 241	Women	Men
Gender (M/W)	(%)		n: 139 (57.7%)	n: 102 (42.3%)
Age (years)	*Mean ± SD*	**58.2 ± 8.2**	**58.4 ± 7.6**	**57.9 ± 8.9**
	Median [IQR]	60.0 [53.0-64.0]	60.0 [53.5-64.0]	59.0 [53.0-65.0]
	Min-Max	30.0-70.0	32.0-70.0	30.0-70.0
MoCA score (0-30)	*Mean ± SD*	**25.2 ± 3.5**	**25.2 ± 3.8**	**25.2 ± 3.2**
	Median [IQR]	26.0 [23.0-28.0]	26.0 [23.2-28.0]	26.0 [23.0-27.0]
	Min-Max	13.0-30.0	13.0-30.0	13.0-30.0
HbA1C (%)	*Mean ± SD*	***8.6 ± 1.3***	***8.5 ± 1.3***	***8.7 ± 1.3***
	Median [IQR]	8.2 [7.6-9.2]	8.2 [7.6-9.1]	8.2 [7.7-9.2]
	Min-Max	7.1-13.5	7.1-12.5	7.1-13.5
Diabetes duration (years)	*Mean ± SD*	**13.5 ± 8.1**	**14.3 ± 8.7**	**12.5 ± 7.1**
	Median [IQR]	12.0 [7.0-19.0]	13.0 [7.0-20.0]	11.0 [6.2-17.0]
	Min-Max	2.0-45.0	2.0-45.0	2.0-30.0

Figure 3. Average tonal audiogram of the study population

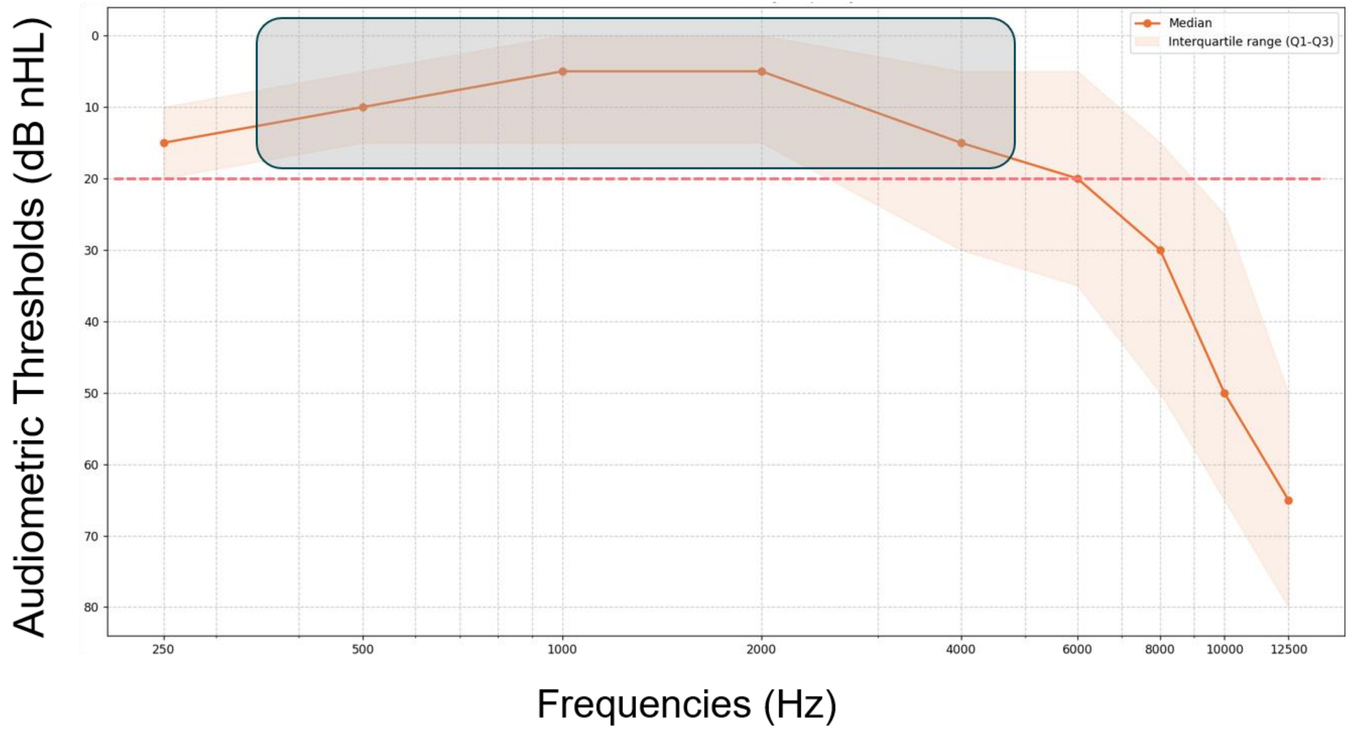


Figure 4. Distribution of PTAv (0.5-4 kHz) in relation to age/sex normative values (ISO7029)

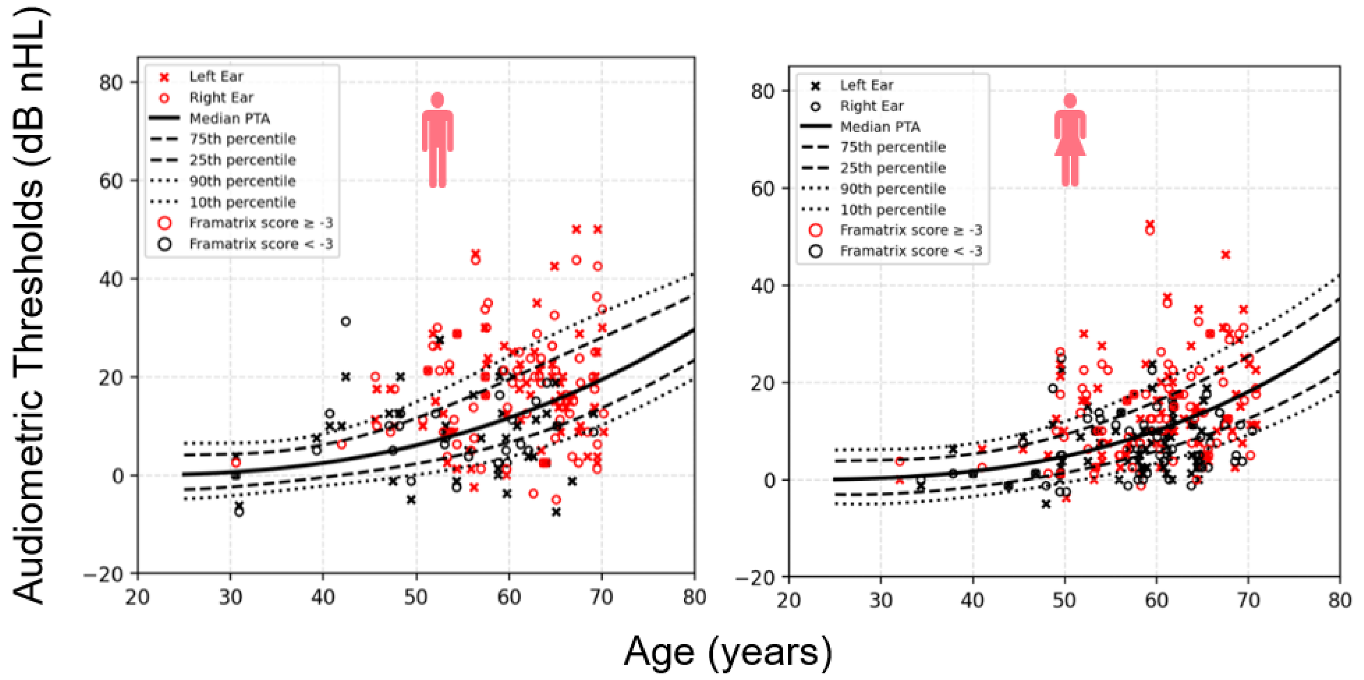
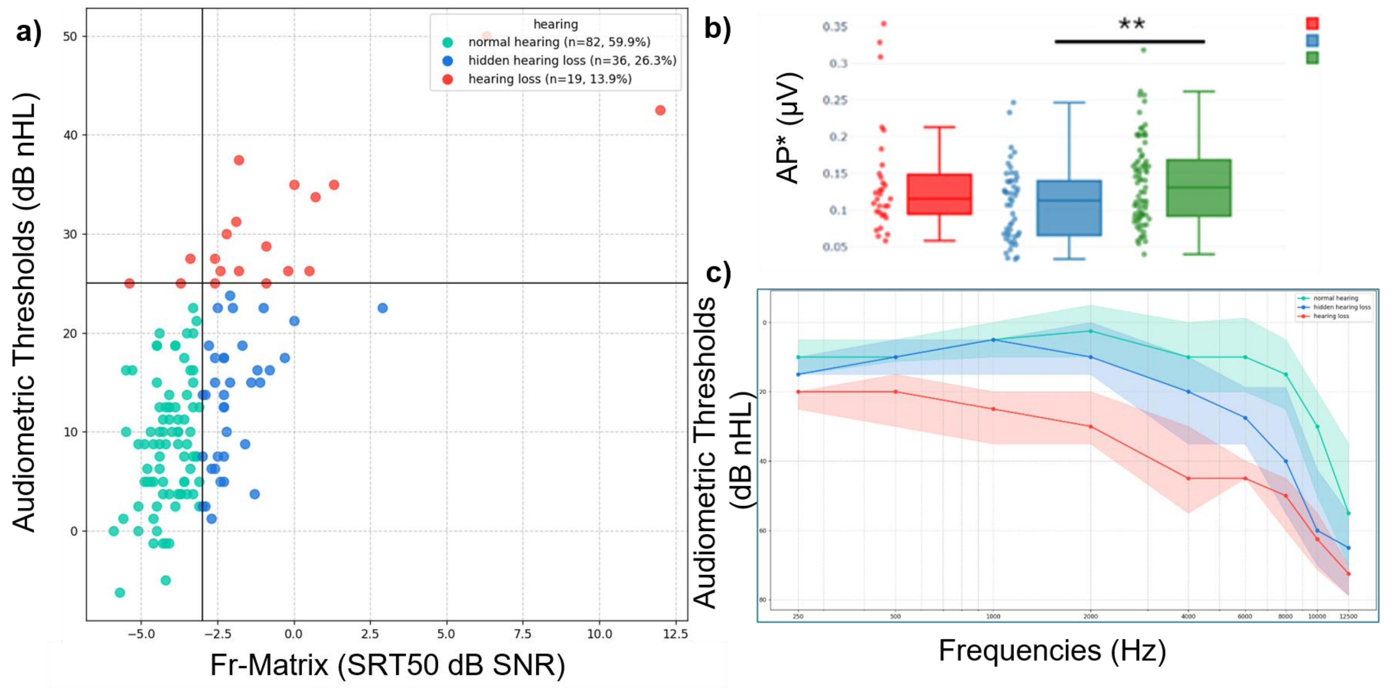


Figure 5. Prevalence of hidden hearing loss (a), and contributions of auditory nerve activity – AP* (b) as well high and extended-high frequency hearing thresholds (c).



RESULTS

- The **prevalence of hearing loss was estimated at 24.5%** (according to BIAP criteria, average threshold 0.5-4 kHz greater than 20 dB nHL) or 17% (according to international criteria, average threshold 0.5-4 kHz greater than 25 dB nHL). (Figure 3)
- However, many participants had **speech intelligibility problems in noise** (marked in red on Figure 4), with degraded scores on the Fr-Matrix test (pathological value greater than or equal to -3 dB SNR recognized as a criterion for hearing aids).
- **Nearly half of the participants (43%) had an abnormal MoCA score** (below 26), consistent with **mild cognitive impairment**, and speech intelligibility was shown to be statistically significantly associated with the MoCA score (in univariate and multivariate analyses; data not shown) when the latter was below 26.
- To eliminate the cognitive component in the investigation of hidden hearing loss (speech-in-noise intelligibility deficit despite a normal tonal audiogram), **analyses were conducted on participants with a normal cognitive score** (MoCA ≥ 26; n=137 – Figure 2).
- In this subpopulation (population D), **the prevalence of hidden hearing loss**, defined by normal pure-tone audiogram with speech-in-noise intelligibility deficit and normal cognition, was determined to be **26.3%** according to the international hearing criteria for normal hearing (mean tonal threshold < 25 dB nHL) (Figure 5a).
- These participants with hidden hearing loss showed a statistically significant decrease in wave I amplitude (auditory nerve activity) compared to participants with normal hearing (Figure 5b) and a decrease in hearing at high frequencies above 4 kHz (Figure 5c).
- **Diabetes duration, gender and presence of complications** (neuropathy, nephropathy) **were statistically associated with speech- in-noise intelligibility deficit** (data not shown).

CONCLUSIONS

Patients with type 2 diabetes (T2D) are more affected in speech-in-noise intelligibility (26.3% of participants) than hearing thresholds at typical frequencies (0.5-4 kHz). This impaired speech comprehension in noise is associated to a decreased hearing acuity at high (and very high) frequencies and a reduced auditory nerve activity in response to suprathreshold sound stimuli.
These symptoms are associated with a longer duration of diabetes and the presence of other complications (peripheral neuropathy, retinopathy).
These results support the possibility of **early auditory neuropathy** leading to **auditory nerve damage** (**possibly cochlear synaptopathy**).
The management of patients with T2D should include **regular hearing screening with speech intelligibility testing in noise, as well as cognitive assessment.**

1. Samocha-Bonet, D., Wu, B. & Ryugo, D. K. Diabetes mellitus and hearing loss: A review. *Ageing Research Reviews* **71**, 101423 (2021).
2. Al-Rubeaan, K. *et al.* Hearing loss among patients with type 2 diabetes mellitus: a cross-sectional study. *Ann Saudi Med* **41**, 171–178 (2021).
3. Baiduc, R. R. & Helzner, E. P. Epidemiology of Diabetes and Hearing Loss. *Semin Hear* **40**, 281–291 (2019).
4. Giraudet, F. *et al.* Impaired auditory neural performance, another dimension of hearing loss in type-2 diabetes mellitus. *Diabetes & Metabolism* **48**, 101360 (2022).

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