AUDITORY DYSFUNCTION IN FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY TYPE 1: BEYOND THE INNER EAR INVOLVEMENT

To the Editor: We read with interest the article titled ''Dysfunction Is a Frequent Feature of Facioscapulohumeral Muscular Dystrophy Type 1 (FSHD1)'' by Frezza et al. (1), recently published in Otology and Neurotology.

The above-mentioned study highlights that cochlear dysfunction may be the cause of the hearing loss in patients affected by FSHD. This statement is sustained by means of the investigation of the auditory function with multiple audiometric tests and with otoacoustic emissions.

We recently performed an audiological evaluation of a cohort of 13 patients also with FSHD1 and some additional considerations can be made.

The inclusion criteria of our patients (58.38 ± 8.18 yr; range, 48–74; five women) was self-reported or clinically diagnosed hearing loss (demographic and audiological data of the group present in Table 1). All patients underwent otoscopic evaluation and tympanogram (both normal for the whole cohort), audiometric testing with pure tone audiometry, frequency discrimination measurements, and event related potential P300 latency analysis.

In our cohort, 5/13 (38%) patients reported a self-perceived hearing deficit despite no previous audiological evaluations. Only one patient reported no pathologic results at pure tone audiometry suggest that hearing loss in FSHD1 is a recurrently reported symptom (see Table 1). Noteworthy, a single patient had normal results but was evaluated because he reported hearing problems, most probably subclinical at this point. The analysis of the average results for each frequency revealed a descending configuration for the hearing threshold, with reduced hearing performance for high frequencies (higher than 2 kHz). Even though the pure tone average might be normal, a mild/moderate loss in high frequencies can be perceived by patients, especially when dealing with speech perception.

To further investigate the hearing performance of these patients' frequency discrimination measurements were performed. A set of 10 triplets of tones with equal intensity were presented to patients, at a comfortable listening level. In each triplet, one of the three tones had a different frequency compared with the other two, and patients were asked to identify the different tone. The difference in frequency had three different levels of difficulty for each of the two-frequency ranges (1000 and 2000 Hz). These tests resulted in pathologic in all patients.

The event related potential P300 latency analysis revealed that all patients presented results in line with the hearing threshold. Notably, the impedance audiometry and the test of acoustic stapedial reflexes revealed that only one patient (1/13, 8%) presented normal acoustic stapedial reflexes. Also, the patient with normal hearing threshold presented absence of the acoustic stapedial reflexes.

This observation can be considered interesting while dealing with these patients. In general, while considering a progressive hearing loss, the absence of reflexes is

TABLE 1. *Demographic, genetic, and audiological data of the cohort*

							Right Audiometry						Left Audiometry						
PT	Sex	Age	Ecori Fragment	FSHD Score	Class	Age Onset HL (yrs)	250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz	8000 Hz	250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz	8000 Hz	Reflexes
1	F	68	28 kb	6	B1	66	35	30	10	10	15	55	55	50	55	55	75	70	Absent
2	M	61	38 kb + 31 kb	7	A3	25	20	15	10	25	55	45	20	20	10	15	55	45	Absent
3	F	56	36 kb + 31 kb	4	A2	NPE	15	15	15	10	20	20	15	20	20	10	10	10	Absent
4	M	50	28 kb	6	A 2	NPE	20	20	20	25	65	35	35	30	20	25	70	35	Absent
5	F	74	35 kb	6	A3	NPE	10	10	15	40	55	70	10	10	15	40	65	65	Absent
6	M	61	21 kb	9	A2	58	15	15	15	20	30	40	15	15	20	15	20	15	Absent only at high frequencies
7	F	56	33 kb	8	A2	NPE	25	30	25	45	35	30	20	20	25	45	40	30	Absent
8	F	65	27 kb	2	B2	60	15	15	20	20	40	30	25	20	20	10	20	30	Absent
9	M	60	33 kb	0	C2	56	20	25	20	25	30	45	15	15	10	15	25	25	Absent only at high frequencies
10	M	63	33 kb	3	A2	60	10	10	20	25	65	10	10	10	20	35	50	15	Absent
11	M	48	32 kb	4	A3	45	25	40	40	40	35	35	10	20	20	25	15	10	Absent
12	M	48	32 kb	7	D1	42	10	10	20	30	25	35	15	15	20	45	25	20	Present bilaterally
13	M	49	38 kb + 33 kb	5	A3	NPE	15	15	15	10	30	30	10	15	15	10	30	30	Absent

The result at pure tone audiometry for each frequency is expressed in dB HL.
FSHD indicates facioscapulohumeral muscular dystrophy; HL, hearing loss; NPE, no previous evaluation; PT, patient; yrs, years.

explained by a damage of the cochlea or the neural circuit crucial for the maintenance of this function. In the case of FSHD1, a hereditary muscle disease, the clinician should also consider the inefficiency of the contraction of the stapedial muscle as a possible cause of reflexes. So, even in patients with slight hearing loss, the stapedial reflexes can be absent due to the reduced function of this structure of the middle ear. Consequently, the absence of reflexes should not be considered a sign confirming a cochlear or retrocochlear nature of hearing loss.

Noteworthy, 2/13 (15%) patients (number 1 and 11) presented an asymmetric hearing loss. This result may be due to the concomitant occurrence of other pathologic processes or to an asymmetric development of an FSHD1-related hearing loss that should be investigated over time.

All the above-mentioned considerations added to the observations made by Frezza et al. (1) lead to the conclusion that hearing loss should be considered a frequent feature of FSHD1, but a thorough evaluation is necessary to ascertain the degree and the impact of the deficit. Even if the recent studies have shown novel findings concerning FSHD1 (2), conclusive data about hearing loss are not available and only future research will help in better defining this issue.

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Ethical Approval: All procedures performed in the 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 for each patient.

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REFERENCES

1. Frezza E, Fuccillo E, Petrucci A, et al. Cochlear dysfunction is a frequent feature of facioscapulohumeral muscular dystrophy type 1 (FSHD1). *Otol Neurotol* 2021;42:18–23.
2. Vercelli L, Mele F, Ruggiero L, et al. A 5-year clinical follow-up study from the Italian National Registry for FSHD. *J Neurol* 2021;268:356–66.

RESPONSE TO LETTER TO THE EDITOR ''AUDITORY DYSFUNCTION IN FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY TYPE 1: BEYOND THE INNER EAR INVOLVEMENT'' BY GHELLER ET AL

In Reply: We read with interest the Letter to the Editor entitled ''Auditory dysfunction in Facioscapulohumeral Muscular Dystrophy Type 1: beyond the inner ear involvement'' by Gheller et al. (1), reporting further evidence of an auditory impairment in patients affected by Facioscapulohumeral Muscular Dystrophy Type 1 (FSHD1).

In particular, Gheller et al. performed various audiological examinations, including speech evaluation tests, frequency discrimination and event related potential (P300) latency analysis, highlighting the presence of a hearing impairment in a population of 13 patients affected by FSHD1, for frequencies higher than 2 kHz. In our recent study on 26 FSHD1 patients, we reported a general alteration of otoacoustic emissions (OAEs) analysis, irrespective of the degree of muscular involvement, suggesting a primary cochlear dysfunction as a typical feature of this disease (2). Altogether, these findings further indicate the existence of a complex involvement of the auditory pathways in FSHD1.

Based on our findings, we suggest to maintain strict exclusion criteria when recruiting patients for such studies to avoid a possible bias of patient's selection and considering not only those subjects who complain about hearing problems, but all FSHD1 subjects. This approach may reveal a possible subclinical hearing dysfunction still unrecognized by the patient.

Further studies are needed to evaluate hearing outcomes in the light of the progression of the disease and to better understand possible correlations between auditory impairment, muscular balance and genetic features.