AUDITORY PHENOTYPE OF INDIVIDUALS WITH INFRATENTORIAL (CLASSICAL) SUPERFICIAL SIDEROSIS: A CROSS-SECTIONAL STUDY

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INTRODUCTION

Infratentorial (classical) superficial siderosis (iSS) is a rare neuro-otological disorder resulting from chronic extravasation of blood into cerebrospinal fluid (often due to dural defects) and deposition of iron-degradation product haemosiderin on the surfaces of CNS structures.

Susceptibility-weighted MRI is the reference standard diagnostic modality.

Infratentorial structures (cerebellum and brainstem) are most commonly involved, as well as the 8th cranial nerves. Supratentorially, Sylvian fissures can be involved[1,2] (**Figure 1**).

iSS-related hearing impairment is predominantly downsloping, resembling age-related changes, and of mixed (sensory end-organ/cochlear or neural) origin.[3] Central auditory (brainstem and beyond) involvement was described in a case report[4].

It is difficult to ascertain the affected segment of the auditory pathway in individuals with iSS due to often small cohort numbers or limited test battery[5].

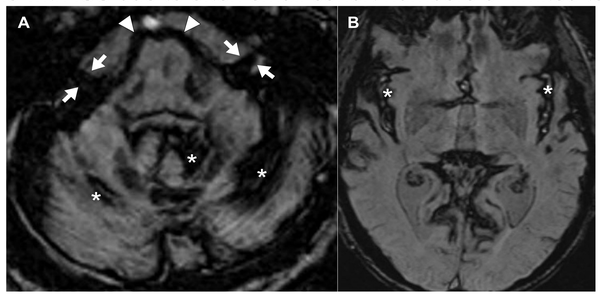

Figure 1. Axial susceptibility-weighted MR images with signal loss (consistent with hemosiderin deposits) involving **A:** cerebellum (asterisks), 8th cranial nerves (arrows) and brainstem (arrowheads); **B**: Sylvian fissures (asterisks).

AIM

To phenotype auditory function in a large cohort of iSS and identify the likely involved auditory structures.

METHODS

Permission for the study was obtained from the departmental clinical governance team (as part of clinical audit).

Patients were also invited to participate in a dedicated research study; permission from the NHS Research Ethics Committee was granted (REC 19/LO/1162AM01).

We reviewed results of auditory assessments of patients with radiologically confirmed diagnosis of iSS between 30/6/2004 and 01/09/2023.

Auditory testing took place at the UCLH NHS Foundation Trust, in line with the BSA guidelines.[5-7]; the results were compared to departmental or published or equipment manufacturers' norms.[8-11]

Relevant anatomy, tests procedures and equipment are described elsewhere.[11] Data were anonymised at extraction.

Each case was reviewed separately for evidence of end-organ sensory, neuronal or central involvement.

Statistical analysis performed using SPSS (v26-28, IBM, Armonk, NY). We tested for association between hearing levels and disease duration (time interval from causative event to test) using Spearman correlation.

RESULTS

N=39, 27 (69%) males

- Of 96 iSS patients, 46 (48%) had auditory tests
- 7/46 (15%) cases were excluded due to unilateral assessments (due to cochlear implantation or previous surgery for vestibular schwannoma in 5 cases) or notes not retrieved (2 cases)
- In 5/39 (13%) only pure tone audiometry (PTA) was available for analysis
- In 4/39 (10%) information was retrieved from clinical letters

	Mean	Median	Standard deviation	Interquartile range
Age at test, years	50.6	56.0	17.5	29.5
Disease duration (n=35), years	21.7	21.5	9.5	13.0
3FA (0.5/1/2 kHz), dB HL	50.3	45.0	32.2	52.1
4FA (0.5/1/2/4 kHz), dB HL	54.1	51.3	31.7	49.4

- There was no meaningful correlation between disease duration and hearing levels represented by 3-frequency (3FA) and 4-frequency (4FA) pure-tone averages.
- In addition to PTA (n=39), the following tests were performed: auditory brainstem responses (n=24); otoacoustic emissions (n=16); acoustic reflex thresholds (n=13); Quick Speech in Noise (n=9), speech discrimination (n=6), Listening in Spatialized Noise-Sentences LiSN-S (n=5)

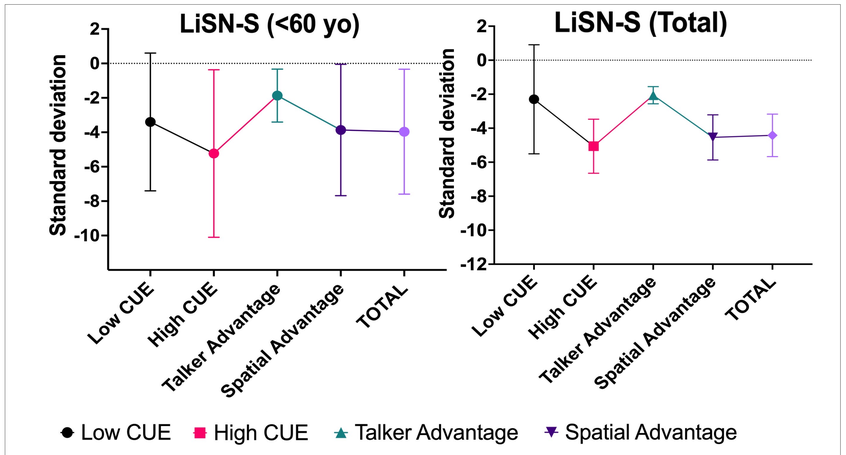

Figure 2. LiSN-S pattern suggestive of spatial processing difficulties. Abnormal (below 2 standard deviations) values were worst in High Cue and Spatial Advantage domains.

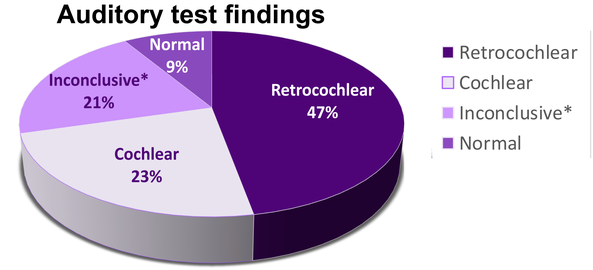

Figure 3. Auditory test findings (n=34). Retrocochlear (neural or beyond) loss was present in n=16, with confirmed cochlear involvement (n=6) or when cochlear loss could not be excluded (n=10). Three patients had bilaterally normal hearing (PTA and at least one other test). Cochlear loss was recorded (n=8) bilaterally, with unilateral retrocochlear involvement (n=2) or inconclusive (n=3) or with no retrocochlear involvement (n=3).
*Results deemed inconclusive (n=7) due to elevated thresholds.

CONCLUSION

Our study included the largest (to date) cohort of iSS patients with auditory assessments.

We demonstrate predominantly retrocochlear origin of iSS-related hearing impairment, with evidence of central auditory dysfunction.

Hearing impairment in iSS may extend proximally beyond the brainstem but further studies are needed to correlate clinical findings with imaging.

References

1. Fearnley JM, Stevens JM, Rudge P. Superficial siderosis of the central nervous system. Brain. 1995;118 (Pt 4):1051-66.
2. Wilson D, Chatterjee F, Farmer SF, Rudge P, McCarron MO, Cowley P, et al. Infratentorial superficial siderosis: Classification, diagnostic criteria, and rational investigation pathway. Ann Neurol. 2017;81(3):333-43.
3. Sydlowski SA, Levy M, Hanks WD, Clark MD, Ackley RS. Auditory profile in superficial siderosis of the central nervous system: a prospective study. Otol Neurotol. 2013;34(4):611-9.
4. Kharytaniuk N, Cowley P, Werring DJ, Bamiou DE. Case Report: Auditory Neuropathy and Central Auditory Processing Deficits in a Neuro-Otological Case-Study of Infratentorial Superficial Siderosis. Front Neurol. 2020;11:610819.
5. Yoo A, Jou J, Klopfenstein JD, Kattah JC. Focused Neuro-Otological Review of Superficial Siderosis of the Central Nervous System. Front Neurol. 2018;9:358.
5. British Society of Audiology. Recommended Procedures, Position Statements, Minimum Training Guidelines and Practice Guidance: The British Society of Audiology; 2016 [Available: https://www.thebsa.org.uk/resources/]
6. British Society of Audiology. Pure-tone air-conduction and bone-conduction threshold audiometry with and without masking: The British Society of Audiology; 2018 [Available from: https://www.thebsa.org.uk/wp-content/uploads/2018/11/Recommended-Procedure-Pure-Tone-Audiometry-August-2018-FINAL.pdf.
7. British Society of Audiology. Tympanometry: The British Society of Audiology; 2013 [Available from: https://www.thebsa.org.uk/wp-content/uploads/2013/04/Tympanometry-1.pdf.
8. Otodynamics. ILO V6 Clinical OAE Analysis and Data Management - User Manual. 2015.
9. Davis AC. Hearing in adults: the prevalence and distribution of hearing impairment and reported hearing disability. . London: Whurr; 1995. xv,1011 p.
10. Cameron S, Glyde H, Dillon H. Listening in Spatialized Noise-Sentences Test (LiSN-S): normative and retest reliability data for adolescents and adults up to 60 years of age. J Am Acad Audiol. 2011;22(10):697-709.
11. N Kharytaniuk, Clinical and imaging biomarkers of audiovestibular function in infratentorial superficial siderosis. 2023. E-Thesis. [available in UCL Discovery: https://discovery.ucl.ac.uk/id/eprint/10163608/]

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