Royal National Throat, Nose and Ear Hospital

University College London Hospitals
NHS Foundation Trust

uclh

BINAURAL SPEECH PROCESSING, TEMPORAL RESOLUTION AND REPORTED HEARING DIFFICULTIES IN GENETICALLY CONFIRMED FRIEDREICH'S ATAXIA PATIENTS

Nehzat Koohi[1,2], PhD; Paola Giunti[3,4], PhD; Gilbert Thomas-Black[3,4], PhD; Doris-Eva Bamiou[1,2,5], PhD

1 The Ear Institute, University College London, London, UK; 2 Neuro-otology Department, University College London Hospitals, London, UK; 3 Department of Clinical and Movement Neurosciences, Institute of Neurology, University College London, London, UK; 4 Ataxia Centre, National Hospital for Neurology and Neurosurgery, University College London Hospitals, London, UK; 5 Biomedical Research Centre, National Institute for Health Research, London, UK

Background

Auditory Neuropathy (AN) refers to the impairment of listening ability caused by disordered conduction in the auditory nerve with relatively preserved outer hair cell function and cochlear amplification. One of the few conditions that affects the auditory nerve is a neurodegenerative disease called Friedreich's Ataxia (FRDA). FRDA is the most frequent autosomal recessive inherited ataxia caused by mutations in the FXN gene. Cardinal features of FRDA are ataxia of both trunk and limbs along with cerebellar dysarthria, global areflexia, deep sensory loss, and pyramidal signs (Dürr et al., 1996). Apparent sensorineural hearing loss, as shown on pure-tone audiogram, is less frequent (Lynch et al., 2002) and has been reported in 8-13% of FRDA individuals (Harding, 1981; Dürr et al., 1996).). Abnormal auditory neural and brainstem responses as a result of axonopathy in the eighth nerve and auditory brainstem, termed as "auditory neuropathy" has been reported in a high proportion of affected FRDA individuals (Jabbari et al., 1983; Rance et al., 2008; Santarelli et al., 2015). Disruption of neural synchrony can have significant effects on auditory perception in listeners with FRDA and impaired temporal resolution and major consequent deficits in speech discrimination in the majority of these patients (Rance et al.,2010).

Herein, we show the auditory phenotypic variability in 15 genetically confirmed FRDA patients.

Results

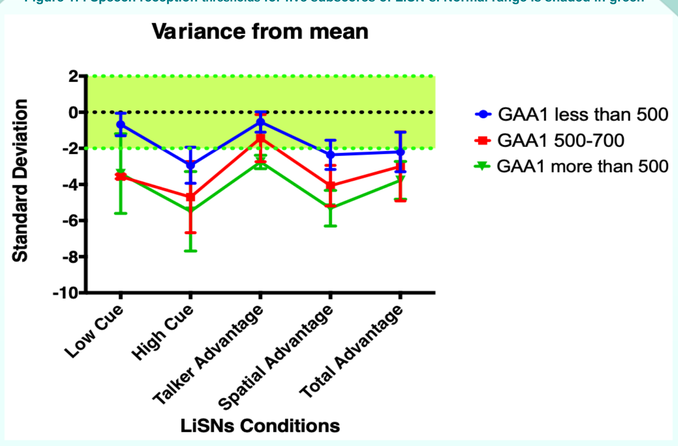
Hearing assessment of five FRDA patients with GAA1 repeats less than 500 revealed no/mild hearing impairment. Mild/moderate hearing impairment was observed in 10 patients with GAA1 repeat lengths of more than 500.

Auditory spatial processing disorder is present in 90% of our FRDA patients, making it impossible for them to focus selectively on sounds coming from one direction while supressing sounds coming from other directions. Deficits in temporal resolution, which is inability to follow rapid changes in a sound, existed in more than 80% of our patients. In a scale questionnaire, SSQ, we received reports of functional hearing difficulties, concerning speech, spatial and hearing quality in a range of complex listening situations that are part of daily living, from most of our FRDA patients. The presence and robustness of otoacoustic emissions suggested intact peripheral hearing in all of our FRDA patients.

Table 1: 2 Baseline audiological assessment details in FRDA patients

Subject	Right OAEs	Left OAEs	Right ABR	Left ABR
FRDA 1	Present	Present	Present	Present
FRDA 2	Present	Present	Present with reduced amplitude	Present with reduced amplitude
FRDA 3	Present	Present	Present	Absent
FRDA 4	Present	Present	Present with reduced amplitude	Present with reduced amplitude
FRDA 5	Present	Present	Present	Present
FRDA 6	Present	Present	Absent	Absent
FRDA 7	Present	Present	Absent	Absent
FRDA 8	Present	Present	Absent	Absent
FRDA 9	Present	Present	Absent	Absent
FRDA 10	Present	Present	Absent	Absent
FRDA 11	Present	Present	Absent	Absent
FRDA 12	Present	Present	Absent	Absent
FRDA 13	Present	Present	Absent	Absent
FRDA 14	Present	Present	Absent	Absent
FRDA 15	Present	Present	Absent	Absent

Figure 1: . Speech reception thresholds for five subscores of LiSN-s. Normal range is shaded in green



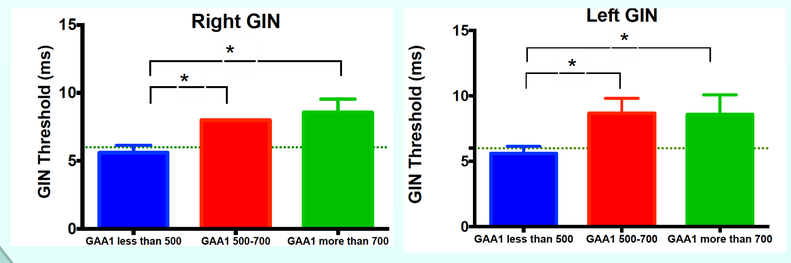


Figure 2: . GIN results in FRDA patients. * p<0.05. KEYS: GIN, gaps in noise test

Methods

Fifteen patients with genetically confirmed FRDA who were homozygous for GAA expansions in intron 1 of FXN gene underwent:

Baseline audiological assessment:

1. Pure-tone audiometry
2. Otoacoustic Emissions
3. Auditory Brainstem Responses

Auditory processing evaluation:

1. Gaps in Noise Test (GIN)
2. Listening in Spatialized Noise-Sentences Test (LiSN-S)

Patient-reported hearing difficulties

1. The Speech, Spatial, and Qualities of Hearing' (SSQ) questionnaire

Age at assessment ranged from 17 years to 48 years (30.8±9.9 years). The number of GAA repeats ranged from 100 to 1200. The mean numbers of GAA repeats on the smaller and the larger alleles were 614±257 and 825±218, respectively. Patients were classified into three groups, those with GAA1 repeats over 700, those between 500 and 700, and those with repeats under 500 (Dürr et al., 1996).

Discussion

We conducted baseline audiological and auditory processing assessment on 15 genetically confirmed FRDA patients. We observed binaural impaired speech perception in 14 out of 15 FRDA patients. However, severity of spatial processing impairment was in varying degrees and strongly associated only with the repeat length of GAA1. Worse talker advantage was observed in FRDA individuals whose GAA1 repeat length exceeded 700. This may reflect frequency discrimination deficits in that talker advantage is dependent on the pitch and timbre characteristics of the speaker (Glyde et al., 2013). The findings of our study suggest that temporal distortion is mainly observed in FRDA individuals with the GAA1 more than 500. All patients whose GAA1 was more than 500 reported gross functional deficits in a variety of complex listening situations typical of those encountered in everyday life (evident on the speech, spatial and qualities of hearing scale questionnaire). In summary, the findings of our study suggest more severe temporal resolution and more degraded neural sound conduction leading to more problems with speech perception and spatial processing in those patients with the GAA more than 500.

References

1. Dürr, A., Cossee, M., Agid, Y., Campuzano, V., Mignard, C., Penet, C., Koenig, M. (1996). Clinical and Genetic Abnormalities in Patients with Friedreich's Ataxia. New England Journal of Medicine.
2. Glyde, H., Cameron, S., Dillon, H., Hickson, L., & Seeto, M. (2013). The effects of hearing impairment and aging on spatial processing. Ear and Hearing.
3. Jabbari, B., Schwartz, D. M., MacNeil, D. M., & Coker, S. B. (1983). Early abnormalities of brainstem auditory evoked potentials in Friedreich's ataxia: evidence of primary brainstem dysfunction. Neurology.
4. Lynch, D. R., Farmer, J. M., Balcer, L. J., & Wilson, R. B. (2002). Friedreich ataxia: effects of genetic understanding on clinical evaluation and therapy. Archives of Neurology.
5. Rance, G., Corben, L., Barker, E., Carew, P., Chisari, D., Rogers, M., Delatycki, M. B. (2010). Auditory perception in individuals with friedreich's ataxia. Audiology and Neurotology.
6. Rance, G., Fava, R., Baldock, H., Chong, A., Barker, E., Corben, L., & Delatycki, M. B. (2008). Speech perception ability in individuals with Friedreich ataxia. Brain.

Acknowledgement

We acknowledge the financial support of the Deafness and Hearing Problems theme NIHR UCLH Biomedical Research Centre (BRC). We would like to thank our patients and colleagues at the Ataxia Centre and Neuro-otology Department of the University College London Hospitals.