



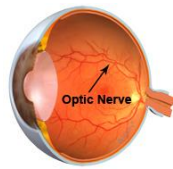
LHON: a qualitative study on the experiences and hopes of patients and caregivers

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Background

- LHON (Leber's Hereditary Optic Neuropathy) is a rare orphan mitochondrial disease, maternally inherited, with an estimated prevalence $\approx 1:30-40,000$ ³, and predominantly affecting males (80%), typically from 15 to 35 years of age.
- In $\sim 90\%$ of cases, LHON is due to mutations in *ND1*, *ND4* or *ND6* genes which encode proteins of the respiratory chain Complex I (CI). Dysfunction of the mitochondrial respiratory chain CI is the direct cause of apoptotic death of retinal ganglion cells and atrophy of the optic nerve.
- The *ND4* G11778A mutation is responsible for the majority of cases ($\sim 70\%$). All mutations have incomplete penetrance.⁴
- Vision loss manifests with acute to sub-acute decline in one eye, with rapid loss to nadir in days to weeks. 50% of patients have their 2nd eye clinically affected by LHON within ≤ 8 weeks of onset.
- Visual prognosis is very poor: between 75 and 98% of patients are reported to have final visual acuity of worse than 20/200, qualifying for legal blindness.⁵
- There is currently no approved treatment and no cure for LHON.



Purpose

- Perceptions of affected patients with the *ND4* G11778A mutation and caregivers* about the diagnostic process, the consequences of LHON on their respective lives & expectations around future treatments have not yet been surveyed.
- The aim of the present study was to gain a deeper qualitative understanding around these themes.

Methodology

- 8 face-to-face exploratory qualitative focus groups took place in November 2014 in 4 countries - USA, UK, Germany and France.
- 1 separate group with LHON patients and 1 with caregivers were set up in each country, all audio and video recorded for further analysis.
- 17 LHON patients with the *ND4* G11778A mutation in total were involved; 13 males and 4 females, aged between 18 and 67 years old.
- 17 caregivers whose relative(s) have LHON participated; 9 mothers, 3 wives, 2 husbands & 1 father.
- Each group was conducted in a viewing facility led by an independent, experienced moderator to guarantee anonymity & confidentiality.
- A semi-structured discussion guide was used & the data collected was analyzed to determine key qualitative trends.

*Caregiver: the word 'caregiver' in the context of this research typically describes relatives or partners providing part or full time support to a patient. We acknowledge that most patients typically thrive for an as independent and autonomous life as possible and, in absence of a better word, we use this term here only reluctantly as patients might find the word 'caregiver' somewhat patronising or labelling

Key findings

Lengthy, worrisome, difficult journey before being diagnosed

- Patients first noticed a relatively quick, but progressive, blurred vision for one eye that they usually related to fatigue, worsening of eye deficiency or ageing; including some patients aware of LHON family history.
- When their vision did not improve, even deteriorated, and started affecting daily activities, patients worried more and usually first consulted an optometrist (USA, UK) or a community-based ophthalmologist (FRA, GER).
- After some visual tests, most patients were told the cause was unexplained, unclear or related to their lifestyle (e.g. smoking) - one was even misdiagnosed with a retina-related condition.
- Others were referred to a hospital-based ophthalmologist for further investigation, a few to a neurologist, leading for one patient to misdiagnosis of multiple sclerosis.
- Patients consulted between 2 and 7 different clinicians, often on their own initiative or pushed by relatives, before being finally referred to a LHON specialist, mainly when the 2nd eye became affected (Fig1).
- After genetic testing, the LHON diagnosis was announced, devastating patients & caregivers who additionally learned that preventing vision loss progression or restoring vision was currently impossible.
- From the first symptoms, it took between 3 and 12 months to diagnosis; typically less time for patients with family history of LHON while more time for females & patients with onset after the age of 35.

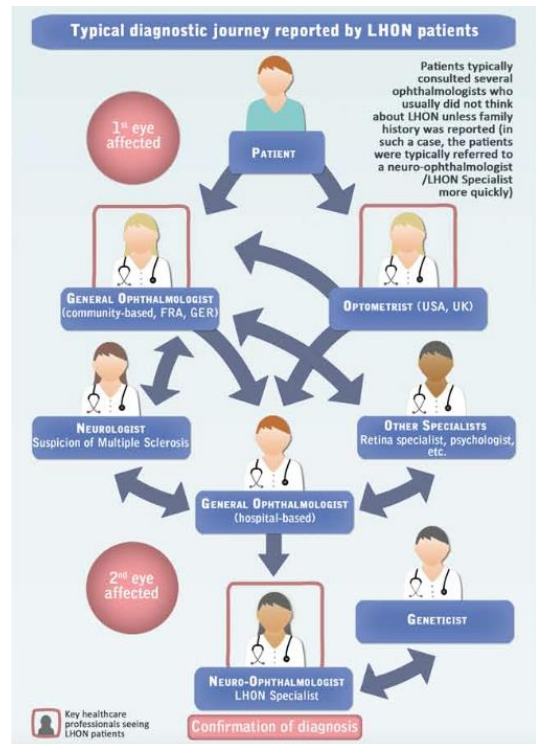


Fig 1. Typical diagnostic journey reported by LHON patients

LHON strongly affects quality of life for both patients and caregivers

- All interviewed patients, including those recently diagnosed with some retained central vision, stress they feel locked in a world apart, often described as gloomy, shapeless, poorly colored if at all (Fig 2).
- This vision loss makes identification of people, objects and situations very complicated for them, requiring permanent attention and vigilance, often leading to a mental tiredness.

LHON limits autonomy of patients

- Several dimensions of the LHON patient's quality of life are negatively influenced by the condition, which generates dependency on others, including for patients who underwent rehabilitation and use visual aids (Fig 3).

LHON generates burden for caregivers

- Caregivers are strongly involved in the LHON's patient life and all had to fit their personal activities around the needs of the patient, some even had to completely sacrifice such activities to be able to fully support their loved one (Fig 4).



Fig 2. LHON patients' quotes, extracted from interviews

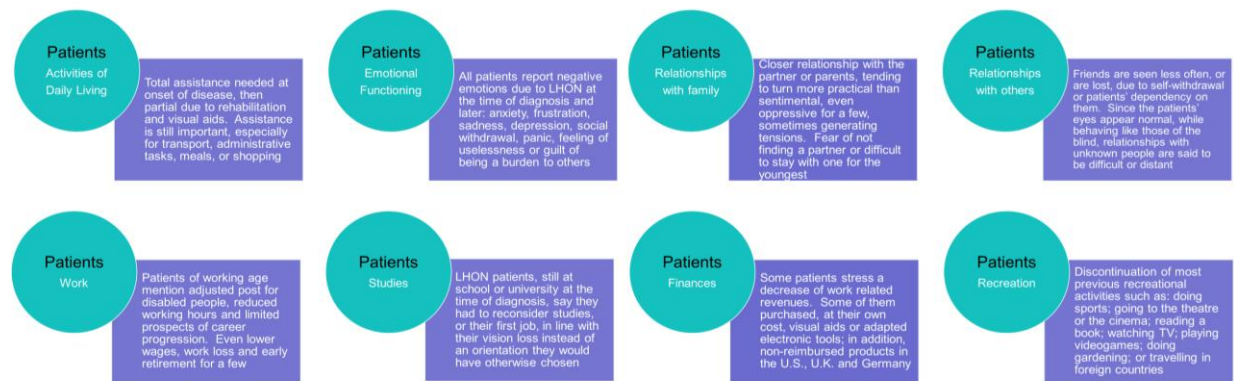


Fig 3. LHON patients' dimensions affected by the condition

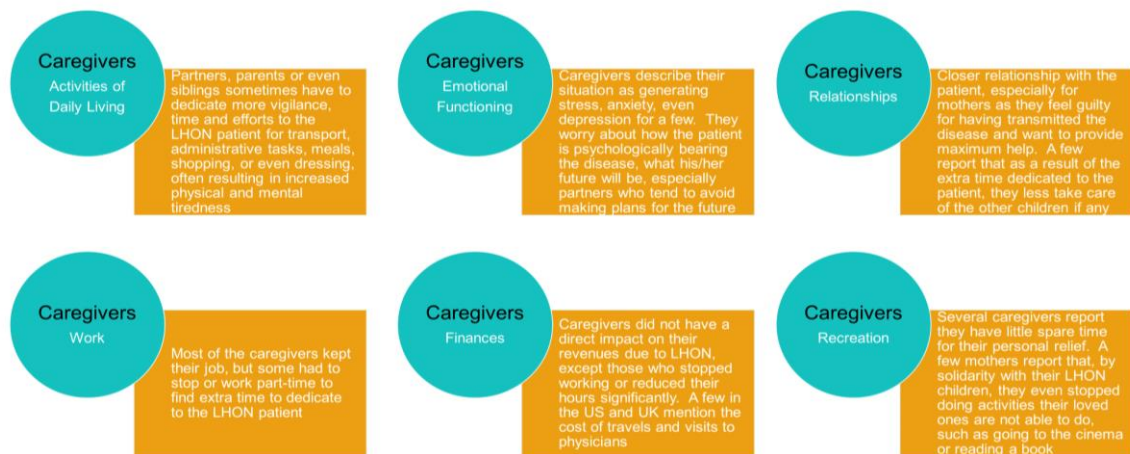


Fig 4. LHON patient caregivers' dimensions affected by the condition

Expectations towards treatments relate to the restoration of some autonomy

- All patients and caregivers wish for a cure. If that is not attainable, then a therapy should improve the vision enough to enable a minimal level of autonomy for patients, as well as less burden for caregivers.
- Enabling daily living activities, facilitating relationships with others in general, relatives in particular, plus being able to go back to previously abandoned recreational activities are the most expected benefits.
- The most hopeful respondents even wish to be able to drive again in the future, which would represent to them the symbol of a fully recovered autonomy.
- Some recently diagnosed patients also wish that a new drug should halt the progression of the vision loss or, even better, restore their initial vision if the medication is taken on time.
- Overall, interviewed respondents admit that just going from 'unable to do' to 'can do with difficulty' would be a big enough breakthrough for them to try out novel treatments.



Fig 5. LHON patients' expectations towards treatment

Conclusions

- The findings highlight that disease awareness among physicians and referral pathways require improvements to lead to relevant diagnosis quicker.
- LHON strongly impacts patients and caregivers' lives as it affects activities of daily living, emotional functioning, relationships, studies, work, recreation and finances.
- Increasing support to patients & caregivers would likely help both improve their quality of life.
- There is an urgent need for an effective drug improving LHON related visual failure to decrease dependency of patients and burden of caregivers.

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