not able to be replicated in adults [95]. Arguably, the protective effect of the stapedial reflex is most efficient in the low frequency range, and may not be as important at frequencies higher than 2 kHz [117, 118]. In short, the protective role of the efferent pathways to cochlea and the possible left-right asymmetries in this system need further research [119, 120].

Clinical relevance of asymmetric NIHL

Unilateral or asymmetrical sensorineural hearing loss is important to discern, as it can be a hallmark symptom/sign of a retrocochlear lesion (i.e. vestibular schwannoma), and in such cases further investigation is required (i.e. MRI scan) unless there is a known reason for the asymmetry [121]. Hence, recognition of asymmetrical hearing due to noise exposure through careful history taking may optimize more appropriate cost-effective investigation of patients.

Conventional teaching suggests that a claimant for compensation who has occupational hearing loss with asymmetrical hearing thresholds is unlikely to have a noise-induced hearing loss in the worse ear, and like any other patient, should be investigated for the 'other' cause of the asymmetry. However, given the multitude of recent evidence in the literature, if the asymmetry under question cannot be explained by causes other than noise, and the MRI scan does not reveal another cause, then the decision given should be in favour of the worker, on the basis of benefit of doubt [94] as the asymmetry may represent a lateral difference in susceptibility to noise damage.

Beyond hearing loss: associated symptomatology

NIHL and tinnitus

The prevalence of tinnitus among noise-exposed workers is much higher (24%) than the overall population (14%) [122], and is exponentially higher in those in the military, up to 80% [123]. Although the majority of individuals with NIHL present with bilateral tinnitus, unilateral tinnitus is reported as well, with a prevalence of up to 47% [124–126]. Tinnitus is more prevalent on the left side [124, 125] consistent with the asymmetry documented in NIHL. The severity of the tinnitus may be associated with the degree of NIHL [126, 127]. The impact of tinnitus has been demonstrated: apart from tinnitus being associated with other comorbidities, such as anxiety, depression and sleep disorders [128], noise-induced tinnitus negatively effects the quality of life in workers [129] and for military personnel, tinnitus can be distracting during a military operation [123].

NIHL and vestibular dysfunction

There is increasing evidence for noise-induced vestibular deficiency, through a mechanism of noise-induced damage to the sacculocolic reflex pathway and/or damage to the vestibular hair cell cilia [62, 130]. This is supported by multiple studies in human and animals.

In humans, several studies, with relatively small sample sizes (n = 20-30), showed that abnormal (reduced, delayed or absent responses) cervical vestibular evoked myogenic potentials (VEMPs) and ocular VEMPs are associated with chronic or acute acoustic trauma [62, 131–133]. This supports the hypothesis that noise causes functional damage to the otolithic organs either directly or indirectly. Also, an association was found between cervical VEMPs and hearing outcome after acute acoustic trauma, therefore it was concluded that abnormal VEMPs might indicate more severe trauma and as a result poorer hearing recovery [62].

Apart from the otolithic organs, noise induced trauma has been shown to cause substantial stereocilia bundle loss and reduction in baseline firing rates of (horizontal and superior) semicircular canals in animal studies [130, 134]. A study of 258 military males identified a strong correlation between vestibular symptoms and abnormal findings on electronystagmography (ENG) testing; the presence of spontaneous, gaze-evoked or positional nystagmus and reduced caloric responses in the worst hearing ear was demonstrated, with significantly more abnormal results of all ENG tests in the asymmetrical NIHL group compared to the group with symmetrical NIHL [135]. In these patients, reduced caloric responses were measured in the worst hearing ear, with the left ear being more often affected, suggesting that acoustic trauma can cause asymmetric noise-induced vestibular loss. Whether or not individuals with symmetrical hearing loss also have bilateral symmetrical vestibular hypofunction cannot be gleaned from the data as absolute values were not reported. Data from this study not only supports the hypothesis that acoustic trauma can cause damage to the (horizontal) semicircular canals, but also shows evidence for asymmetrical trauma after noise exposure, in line with previously discussed evidence for asymmetric induced hearing loss (see paragraph "Asymmetric NIHL").

In animals, noise exposure resulted in a reduction in stereocilia bundle density in vestibular end organs as well as a reduction in regular vestibular afferent baseline firing rates of the otolithic organs and the anterior semicircular canal [130]. As a normal vestbulo-ocular reflex was measured, it was concluded that noise-induced vestibular damage can be present even in the setting of normal vestibular tests; comparable to "hidden hearing loss", this might indicate that noise exposure can also cause "hidden vestibular loss" that cannot be identified due to limitations in current techniques for vestibular assessment. This might explain why normal or marginally abnormal vestibular function tests can be seen in noise-exposed individuals [136, 137]. Although the impact of noise-induced vestibular loss is unknown, it

may explain why individuals with NIHL may present with balance disorders and dizziness [135, 138] and therefore needs to be considered when evaluating the impact of noise-induced trauma.

The socio-economic impact of NIHL

The United States Government Accountability Office report on noise (2011) indicated that hearing loss was the most prevalent occupational health disability in the Department of Defense (DoD) [123]. The DoD civilian worker compensation costs were approximately $56 million in fiscal year 2003, and Veterans Affairs compensation costs were approximately $1.102 billion in fiscal year 2005 with hearing loss as second most common type of disability [12]. The World Health Organization reported that hearing loss is in the top three common health conditions related to disability in the world as of 2017 [139, 140].

The consequences of occupational NIHL to the individual, although not life-threatening, can be dire. Hearing loss limits an individual's ability to communicate with the surrounding world, which can lead to increased social stress, depression, embarrassment, poor self-esteem, and relationship difficulties [59]. Social handicap resulting from communication difficulties is exacerbated in difficult listening situations, such as environments with excessive background noise. In addition, longitudinal studies have demonstrated an association between hearing loss and declines in cognition, memory, and attention signifying the importance of prevention and treatment of hearing loss [141, 142].

Occupational NIHL has been associated with an increased risk for work-related injuries. For each dB of hearing loss, a statistically significant risk increase was observed for work-related injuries leading to admission to hospital [143]. Individuals with asymmetrical NIHL may experience decreased ability to localize sounds, which is critical in certain groups of workers like firefighters and other public safety workers, and can be a career-ending disability that has public safety implications as well [144].

Non-pharmaceutical interventions

Education, regulations, legislation and workplace noise policy

Prevention remains the best option for limiting the effects of acoustic trauma. Hearing conservation programs in elementary school children are potentially effective to increase the knowledge about the hazards of noise exposure early in life and this may result in behavioral changes towards noise reduction and ear protection [145]. For industrial noise, elimination or reduction of noise through engineering or administrative controls is the best line of defense. Legislation on occupational noise exposure help to regulate noise exposure and result in noise reduction and/or noise reducing technical improvements to protect employees [146].

The risk of NIHL can be minimized if noise is reduced to below 80 dB(A) (weighted decibel relative to human ear) [147]. For higher levels of noise, regulations are necessary as the extent of biological damage correlates directly to the total sound energy level, a function of sound pressure (decibels) and the duration of exposure (time) [9]. Hearing loss prevention programs establish permissible exposure limits with an exchange rate. The exchange rate defines the number of decibels by which the sound pressure level may be decreased or increased for a doubling or halving of the duration of exposure. This principle is reflected in occupational exposure limits for workplace noise with maximum daily exposure limits halved for every 3–5 dB increase in noise intensity. For instance, assuming an exchange rate of 3 dB, 4 h of exposure at 88 dB(A) is as equally hazardous as 8 h at 85 dB(A).

A recent Cochrane review concluded that in order to prevent occupational hearing loss, better implementation of legislation and better prevention programs are necessary [148]. Regulations vary widely among different countries and one third of countries in the world still do not have regulations or legislation regarding permissible noise levels and exchange rates [149]. Most North and South American countries have the permissible exposure limit (PEL) of 85 dB(A) for an 8 h work day [149]. In some countries (and some provinces in Canada), the PEL is up to 90 dB(A). As TTSs are higher when workers are exposed to 90 dB(A) as compared to 85 dB(A), a standardized reduction of the PEL to 85 dB(A) should be established in order to reduce the prevalence of NIHL [150]. There is also no international consensus regarding the exchange rate, which varies between countries from 3 dB to 5 dB [149]. There is evidence, however, that 3 dB overestimates the risk of NIHL and that 5 dB is a better fit [151]. For impulse noise, there is most often a limit of peak sound pressure level of 140 dB [152].

Hearing protection

Hearing protection offers a secondary level of protection. However, evidence for effective hearing loss prevention programs (using personal hearing protection) is limited. The most effective hearing protection, including earmuffs and earplugs, can reduce loud noise trauma, but compliance may be limited due to the impact on one's ability to communicate when they are worn and/or discomfort related to their use [153, 154]. To promote the use of hearing protection, different interventional strategies may be beneficial, such as providing general information to motivate workers to use hearing

Neurotrophin-3 (NT3) and brain derived neurotrophic factor (BDNF) are important for formation and maintenance of hair cell ribbon synapses in the cochlea, as well as in the vestibular epithelia [190]. NT3, derived from supporting cells, promotes the recovery of the number of ribbon synapses as well as their function after noise-induced trauma [189, 190]. A dose-dependent effect was found of glial cell-derived neurotrophic factor (GDNF) on sensory cell preservation as well as ABR confirmed hearing threshold, after chronic application of GDNF (10 and 100 ng/ml) through a cochleostomy in the scala tympani via a micro-osmotic pump. However, this effect was small and appears to be associated with some toxicity at a higher concentration (1 μg/ml) [188]. Even a single application of NT3 and BDNF on the round window, immediately after noise trauma, can potentially reduce the synaptopathy (indicated by increased number of presynaptic ribbons, postsynaptic glutamate receptors, and co-localized ribbons) and recover hearing [191]. Another approach is transplantation of neurotrophin-secreting olfactory stem cells into the cochlea, which also caused restoration of noise-induced hearing loss [192]. Although these results are promising, long-term effects are still unknown and no studies in humans have been performed to date.

Other pharmaceutical agents

Other pharmaceutical agents with possible protective NIHL effects include magnesium and statins. A human study [193] as well as research on animal models [194, 195] have shown that acoustic trauma can potentially be minimized by magnesium, as it reduces apoptosis of hair cells by a reduction of calcium flow into the cell, thereby reducing reactive oxygen species formation. A double-blinded, placebo-controlled, crossover trial to assess the effects of prophylactic N-acetylcysteine (600 mg) and magnesium (200 mg) prior to noise exposure is pending [196].

Statins might prevent NIHL by reducing oxidative stress and improving hair cell survival in animals [197, 198]. A significant recovery of TTS (determined by measuring distortion product otoacoustic emissions) was found in rats treated with 5 mg/kg atorvastatin administered daily for 2 weeks prior to 2 h of noise exposure [199].

Surgical treatment

Cochlear implantation

Due to the severity of the hearing loss and/or the poor speech recognition due to synaptopathy, some individuals with NIHL might eventually become candidates for cochlear implantation (CI) either with full electrical or with electro-acoustic stimulation (EAS). Studies have reported NIHL as the etiology of deafness in implanted individuals, with a prevalence ranging from 2% (CI) to 20% (CI with EAS) [200, 201]. This may underestimate the true prevalence, considering the high percentage of unknown etiologies approximating 40–50% of CI recipients [200]. Currently we can only speculate on the extent to which the SNHL in these implanted individuals can be attributed to noise exposure or due to a combination of other underlying predisposing factors.

Conclusion

The impact of noise-induced hearing loss is more widespread than has previously been recognized. Apart from a wide range of hearing frequencies that can be adversely affected by noise exposure, there is increasing evidence that noise-induced synaptopathy causes reduced speech perception in noise, even when pure tone thresholds are still preserved ("hidden hearing loss"). Evidence in the current literature further supports the notion that noise exposure can result in an asymmetric pattern of hearing loss due to unique differences in susceptibility to noise damage within individuals, increase frequency of tinnitus as well as vestibular dysfunction. The left ear (hearing and balance) is more adversely affected by noise, even in the presence of symmetric noise exposure. Future studies should focus on underlying mechanisms that lead to the susceptibility of left-right asymmetry, and to understand the protective role of the efferent pathways to the cochlea as demonstrated in gender differences. Primary prevention with a focus on regulations, legislation and education in schools, in combination with proper hearing protection are important first lines of defense. Further human studies are needed to address the effectiveness of pharmaco-therapeutic options to prevent or mitigate noise-induced trauma.

Abbreviations

ABR: Auditory brainstem response; dB(A): A-weighted decibel; dB: Decibel; ENG: Electronystagmography; kHz: Kilohertz; NAC: N-acetylcysteine; NIHL: Noise-induced hearing loss; OAEs: Otoacoustic emissions; PEL: Permissible exposure limit; PTS: Permanent threshold shift; ROS: Reactive oxygen species; SNHL: Sensorineural hearing loss; SPL: Sound pressure level; TTS: Transient threshold shift; VEMPs: Vestibular evoked myogenic potentials

Acknowledgement

None.

Funding

None.

Availability of data and materials

Data analysed during the current study are publicly available from Pubmed and Google Scholar.

Authors' contributions

TNL: protocol development, collection and analysis of data, manuscript writing and assembly. LS: protocol development, collection and analysis of data, manuscript writing and assembly. JL: protocol development, review of manuscript. BW: protocol development, review of manuscript, final approval of manuscript.

Competing interests

The authors declare that they have no competing interests.