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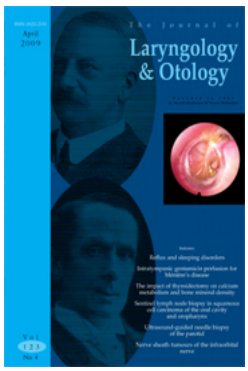

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T H J Draper and D-E Bamiou

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Clinical Record

Auditory neuropathy in a patient exposed to xylene: case report

T H J Draper, D-E Bamiou*

Abstract

Objective: To report the case of an adult patient who developed auditory complaints following xylene exposure, and to review the literature on the effects of solvent exposure on hearing.

Case report: The patient presented with a gradual deterioration in his ability to hear in difficult acoustic environments and also to hear complex sounds such as music, over a 40-year period. His symptoms began following exposure to the solvent xylene, and in the absence of any other risk factor. Our audiological investigations revealed normal otoacoustic emissions with absent auditory brainstem responses and absent acoustic reflexes in both ears, consistent with a diagnosis of bilateral auditory neuropathy. Central test results were also abnormal, indicating possible involvement of the central auditory pathway.

Conclusions: To our knowledge, this is the first report of retrocochlear hearing loss following xylene exposure. The test results may provide some insight into the effect of xylene as an isolated agent on the human auditory pathway.

Key words: Auditory Neuropathy; Hearing; Xylene; Solvent Exposure

Introduction

Organic solvents are common in industrial environments and are used in large quantities across the world. Some of the more common solvents include xylene, toluene and styrene and can be found in household items such as paints, pharmaceuticals, adhesives, pesticides and household cleaners. However, research suggests that long term or acute exposure to solvents can have noxious, neurotoxic and ototoxic effects.[1]

Humans with long term or acute exposure to solvents have demonstrated hearing losses greater than would be expected for their age[2–6] and, when working in industrial environments using solvents, greater than would be expected for noise exposure alone.[3–5,7] There is also evidence that solvent exposure may result in retrocochlear rather than peripheral cochlear lesions in humans. For example, impaired speech recognition scores consistent with a retrocochlear pattern and/or abnormal cortical responses and/or abnormal reflex decay have been reported in populations working with toluene,[5] jet fuels,[8] styrene[9] and mixtures of solvents.[8,10–12]

It is now documented that solvents should be considered as individual substances with different specific toxicities,[12] and that solvents may act on transmitters specific for certain neural structures and pathways.[10] For example, significantly delayed auditory brainstem responses (ABRs) were measured in a group of normally hearing workers professionally exposed to toluene.[13]

Xylene is a solvent structurally related to toluene.[14] There is no literature on the effect of xylene, acting as a single agent, on the auditory pathway in humans.

We present a case of an adult patient with hearing loss and auditory complaints attributed to auditory nerve pathology, i.e. auditory neuropathy or dys-synchrony. This patient's hearing complaints developed at the time of xylene exposure, in the absence of any other risk factors for auditory neuropathy or dys-synchrony (as per his medical history).

Case report

A 60-year-old man presented to the otoneurology department with a 40-year history of hearing difficulties. His symptoms had begun in his 20s while researching for his PhD and after exposure to the solvent xylene. He had worked in a small basement hut where xylene leaked into a water tank and escaped into the atmosphere. It was estimated that this exposure had occurred over a six-month period; the basement hut had been small with little or no ventilation.

A few months after the xylene exposure, the patient had noticed problems hearing in the presence of background noise. His symptoms had gradually deteriorated over time. However, he had been discharged from audiology departments on two occasions due to normal pure tone audiometry results. He had been diagnosed with auditory neuropathy or dys-synchrony at the age of 50 years, at which time he had tried both analogue and digital hearing aids but found them of no benefit.

On presentation to our clinic in March 2006, the patient described an inability to hear speech in the presence of noise and to understand people with accents, and the need to lip-read and concentrate when anyone spoke to him. He had given up using the telephone and avoided noisy social situations. The patient had no family history

From the Audiology Department, Royal Sussex County Hospital, Brighton, and the *Neuro-otology Department, National Hospital for Neurology and Neurosurgery, London, UK.
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of early onset hearing impairment. He could not recall any other significant event or illness before his hearing problems began.

The patient's medical history included a right-sided sphenoid wing meningioma removal in October 2005. Due to the tumour's location, it was deemed highly unlikely that this had caused the patient's audiological symptoms. No neurological impairments were identified and the patient had normal nerve conduction. No central nervous system deficits or sense impairment (often associated with solvent exposure) were identified. Previous magnetic resonance imaging and computed tomography (CT) scans, performed following surgery, did not show any residual tumour and were otherwise normal.

Pure tone audiometry and acoustic reflex threshold results are illustrated in Figure 1. In this patient, the combination of absent or raised (>110 dBHL) ipsi- or contralateral acoustic reflex threshold and absent ABR in the presence of otoacoustic emissions was consistent with the diagnosis of bilateral auditory neuropathy or dys-synchrony.[15,16] Maximum speech recognition scores of 66 and 63 per cent at 60 dBHL were present on the right and left respectively, with a significant rollover of 55 and 5 per cent at higher intensities; this was worse than would be predicted from the audiogram.[17] Poor temporal processing was demonstrated by this patient's inability to complete gaps in noise testing,[18] which had to be abandoned due to the patient's random answers (Table I). Central auditory processing tests,[19] which are sensitive to lesions of the central auditory pathway, were abnormal in at least one ear for each test (Table I).

Discussion

This case report presents a sequence of events and facts that may be linked, and the authors are aware that there is no hard evidence of pathology caused by xylene exposure. Our subject was exposed to xylene over a relatively small time scale (six months), and there is no quantitative information regarding the concentration of xylene in the atmosphere at the time (although the laboratory was small and inadequately ventilated). However, Dick reported that there is no real definition of what is regarded as a significant exposure to solvents, and no verdict on whether the important determinant of adverse effects is the lifetime (cumulative) exposure or the peaks (intensity) of exposure.[1] In addition, the subject could have idiopathic auditory neuropathy or dys-synchrony, although the majority of reported cases (80 per cent) present in conjunction with specific medical risk factors and generalised neuropathic disorders.[20] Despite these factors, reporting this case may be of some importance, given the clinical setting, regarding the possible specific toxicity of xylene on the auditory nerve and/or central auditory system in humans.

Auditory neuropathy or dys-synchrony is defined as reduced and/or asynchronous auditory nerve function, in the presence of normal outer hair cell function.[15] The

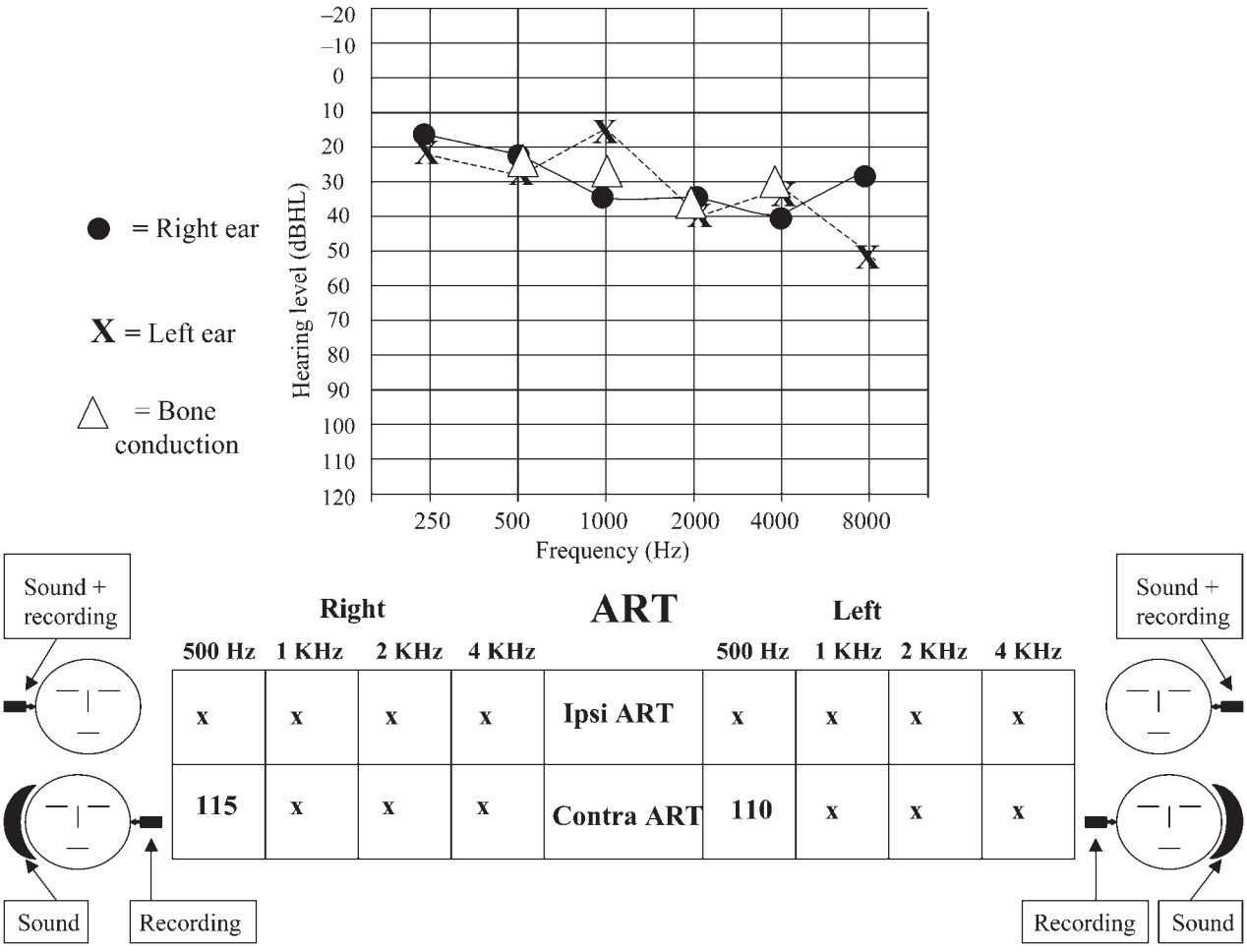

FIG. 1
Pure tone audiogram and acoustic reflexes (ARTs) obtained in March 2006.

TABLE I

CENTRAL AUDITORY PROCESSING TESTS AND RESULTS

Test	Description	Pt response	Score
FPT	Presentation of 3-tone sequence (varied combination of low frequency (880 Hz) & high frequency (1122 Hz) stimuli) 30 trials per ear Pass rate 80% correct	Description of each sequence (e.g. high, low, high)	80% right 53% left
DPT	Presentation of 3-tone sequence (varied combination of a long duration (500 ms) and a short duration (250 ms)) Interstimulus interval = 330 ms 30 trials per ear Pass rate 70% correct	Description of each sequence (e.g. long, long, short)	63% right 73% left
GIN	6-s burst of white noise containing 0–3 gaps varying in duration (2–20 ms) & timing within the noise 36 trials each ear Pass rate: shortest gap detection $\leq$6 ms in at least 50% of trials (i.e. at least 3/6 trials)	Identification of number of gaps heard within noise	Abandoned as patient gave random answers

Pt = patient; FPT = frequency pattern test;[19] DPT = duration pattern test;[19] GIN = gaps in noise test.[18] See text and references for further details.

possible sites of lesion in this condition include the cochlear inner hair cells, the synapse between the inner hair cells and the type I auditory nerve fibres, and the auditory nerve itself.[20] The mechanism of auditory dysfunction may vary between individuals, and is thought to relate to either a dys-synchrony of the auditory nerve (e.g. due to myelin damage) or a reduction in the numbers of neural elements contributing to the volume-conducted response (e.g. due to axon-related neuropathies and inner hair cells lesions).

An inability to follow temporal fluctuations is likely to be the underlying cause for the poor speech recognition experienced by patients with auditory neuropathy or dys-synchrony;[21] this was demonstrated by the inability of our patient to complete gaps in noise testing. The abnormalities detected in the central auditory processing tests may be attributed to disordered auditory nerve input and/or central auditory involvement. However, in view of the potential toxicity of solvents recorded previously at this higher level, central involvement at the level of the auditory cortex cannot be ruled out. Therefore, we may have a mixed picture: intact cochlea, impaired auditory nerve, but also possible impairment at the level of the brainstem and above.

In humans, many studies have investigated the effect of mixed solvents (including xylene) on the auditory system, but none have investigated the effect of xylene acting as a single agent. Xylene is structurally related to toluene,[14] and some human studies have examined the auditory pathways affected by this latter solvent more closely. Morata *et al.* carried out various audiological tests on workers from a printing factory who had been exposed to toluene or mixed solvents.[5] The results demonstrated an interaction between toluene and noise exposure which resulted in a greater risk of hearing impairment. Interestingly, the observed hearing losses were only mild (<40 dBHL) and reflexes were present in most cases. However, the noise plus toluene group had a greater percentage of cases with reflex decay, particularly for contralateral stimulation, compared with ipsilateral stimulation. Morata and colleagues suggested that, in these workers, the observed hearing loss showed an additional central component at the intra-axial brainstem level.

Metrick and Brenner reported the cases of two young adults with neurological disorders secondary to spray paint (toluene) abuse. These patients had high frequency hearing losses and normal reflexes.[6] Their ABRs showed the presence of waves I and II but the absence of later waves, suggesting bilateral lower brainstem dysfunction.[6] Both patients had abnormal CT scans showing evidence of brainstem atrophy.

- **Audiological studies of humans exposed to solvents have demonstrated peripheral hearing losses and/or impairment of the central auditory pathway (i.e. brainstem and above)**
- **Solvents should be considered as individual substances with specific toxicities; however, it is difficult to test for this in humans**
- **This is the first report on the possible effects of xylene acting as a single agent on the auditory pathway in a human with retrocochlear hearing loss**

A study by Abbate *et al.* reported results that perhaps compare most closely to our case. These authors found a significant delay in ABR latencies, and a significant delay in interpeak latencies (compared with a control group) for waves I, III and V at click rates of 11.1 and 90 clicks per second, for workers professionally exposed to toluene.[13] Both groups were controlled for noise exposure and neurological diseases, and all workers had thresholds below 20 dB. Interestingly, waves I–III were more significantly altered than wave V. Central auditory tests were not carried out. Abbate and colleagues proposed that the wave I alterations found could be attributed to the solvent's effect on the peripheral receptor structures of the auditory nerve, because of its liposolubility. This could impair the membrane integrity of the peripheral receptor and/or modify the structure of the junctional site, resulting in alteration of the stimulus transduction mechanism. Xylene is more liposoluble than toluene;[14] due to its

structural similarity, it could be proposed that xylene has a similar mechanism of toxicity on the human auditory nerve.

This is the first report of retrocochlear hearing loss in a human adult patient following xylene exposure and in the absence of any other risk factor. Caution should be noted regarding the length of time the subject was exposed to the solvent, and the fact that no inferences can be made about the concentration or biochemical properties of the solvent. However, the test results may provide some insight into the effect of xylene as an isolated agent on the human auditory pathway.

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Address for correspondence:
Miss Tracy H J Draper,
Audiology Department,
Royal Sussex County Hospital,
Eastern Road,
Brighton BN2 5BE, UK.

Fax: 01273664806
E-mail: tracy.draper@bsuh.nhs.uk

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