

Jet Fuel, Noise, and the Central Auditory Nervous System: A Literature Review

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ABSTRACT Prompted by the continued prevalence of hearing related disabilities accepted as eligible for compensation and treatment under Australian Department of Veterans' Affairs legislation, a review of recent literature regarding possible causation mechanisms and thus, possible prevention strategies, is timely. The emerging thoughts on the effects of a combination of jet fuel and noise exposure on the central auditory nervous system (CANS) have relevance in the military aviation context because of the high exposures to solvents (including fuels) and unique noise hazards related to weapons systems and military aircraft. This literature review aimed to identify and analyze the current knowledge base of the effects of combined exposure to JP-8 jet fuel (or its aromatic solvent components) and noise on the CANS in human populations. We reviewed articles examining electrophysiological and behavioral measurement of the CANS following combined exposures to jet fuel (or its aromatic constituents) and noise. A total of 6 articles met the inclusion criteria for the review and their results are summarized. The articles considered in this review indicate that assessment of the CANS should be undertaken as part of a comprehensive test battery for military members exposed to both noise and solvents in the workplace.

INTRODUCTION

Many sources of potentially damaging noise have long existed in military settings. Some of these sources include weapons systems (e.g., handguns, rifles, artillery pieces, and rockets), wheeled and tracked vehicles, fixed- and rotary-wing aircraft, ships, explosive devices (e.g., bombs, grenades), and communications devices.

Military aircraft operations present unique hazards not encountered in any other occupation and military aviation workers experience exposures that are different from those in the civilian environment. Many military aircraft are unique in their design, flight characteristics, and mission performance. Military aircraft engines, including those on transport aircraft, may use less noise abatement than those on commercial aircraft and may be augmented by afterburners and other military specific components.¹ Military aircraft components such as afterburners also produce intense noise levels well above the legislated exposure guidelines, which can contribute to hearing loss.¹ In addition, it has been demonstrated that aromatic solvents such as those found in jet fuel may enhance the damaging effects of noise, such as that produced by military aircraft, and also increase the risk of hearing loss beyond the risk for noise exposure alone.²

Because of the widespread, albeit erroneous, acceptance that "noise is just part of the job," hearing loss observed in military settings with high levels of solvent and noise is often assumed to be solely due to noise. Epidemiological evidence;

however, indicates that there is a two- to five-fold increase in the risk of hearing loss among humans exposed to aromatic solvents, including those solvents that are the primary constituents of jet propulsion fuel 8 (JP-8), i.e., toluene, xylene, benzene, *n*-hexane, naphthalenes, and aliphatic hydrocarbons.³⁻⁷

Although the deleterious effects of occupational noise on hearing have been well studied, only recently has attention shifted to the individual and synergistic ototraumatic effects of combined chemical and noise exposures. Since first discussed in 1984,⁸ the biological plausibility of noise and chemicals interacting to induce sensorineural hearing loss has now been demonstrated in humans in more than 16 industrial studies. It has been well documented that exposure to hydrocarbon fuels, including JP-8 and kerosene, can induce neurological effects⁹⁻¹¹ and adverse effects on the human central nervous system.^{10,12} This leads to the hypothesis that central auditory nervous system (CANS) dysfunction could also be expected.⁵

The majority of the solvents studied to date cause a loss of auditory sensitivity in the mid-frequencies in rats, affecting outer hair cells in the order of third, second, and then first row of outer hair cells.¹³ Inner hair cells are generally unaffected. Simultaneous exposure to solvents and noise results in a synergistic effect; the pattern of trauma mirrors that due to noise exposure rather than solvents as the pattern of damage due to solvent exposure is not very clear, but is more enhanced. There is a critical level when synergy occurs and findings show that both the peripheral and central auditory pathways can be affected.¹³

Thus, this literature review aimed to identify and analyze the current knowledge base of the effects of combined exposure to JP-8 jet fuels (or its aromatic solvent components) and noise on the CANS in the military aviation population. Noise of any level—not necessarily loud noise over 85 dBA—was considered.

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METHODS

Search Strategy

A literature search was performed using the online database access points of the library of the University of Queensland (Queensland, Australia) to identify peer-reviewed articles published between 1993 and 2014 that examined human exposure to jet fuel or its aromatic solvent components (toluene, xylenes, benzene, *n*-hexane, naphthalenes, and C₉–C₁₂ fractions) and noise on the CANS. Although *Military Medicine* journal guidelines suggest that generally the articles reviewed should have been published within the last 10 years, only one article was identified in the initial search. As such, the search was extended to 15 and then to 20 years to capture the bulk of the very limited literature on this topic. Also, the search was initially restricted to articles relating to military aviation workers, but this resulted in only one article being identified.

Multiple databases were searched including CINAHL, MEDLINE, Proquest, Pubmed, ScienceDirect (Elsevier), TOXLINE, EMBASE, Health Collection (Informit), and Nursing and Allied Health Collection (Gale). Key words used in the search were hearing loss; solvent; noise; electrophysiological; auditory dysfunction; central auditory nervous system; Auditory Brainstem Response, ABR; P300; auditory evoked potentials; acoustic reflexes; auditory pathways and jet fuel. Combinations of the above key words; e.g., solvent induced hearing loss and noise and auditory dysfunction were also used. This initial search was broadened to include jet fuel and/or its aromatic components, and the key words benzene, naphthalene, toluene, and xylene were also used. The searches were confined to English language literature where the full article was available electronically or on request through the university library. The abstract of each article was reviewed, and the relevant article retrieved for further evaluation including a further literature search using the reference lists from the publications identified in the first search.

Article Evaluation

Articles identified in the online search were evaluated using a set of inclusion and exclusion criteria. Articles fulfilling all of the following inclusion criteria were accepted for review:

- (1) Reporting on central auditory dysfunction in humans induced by a combination of noise (of any loudness) and jet fuel or its aromatic solvent components;
- (2) Reporting the use of electrophysiological and/or behavioral measurements of the CANS. Studies investigating pure-tone thresholds were also included, as they reflect the functioning of both the peripheral and central auditory systems; and
- (3) Published in English language, peer-reviewed journals.

Study Inclusion and Exclusion

The initial cross database search of the University of Queensland Library identified 178 citations published between 1993 and 2014. The searches of individual databases through the University of Queensland Library yielded 44 articles using EMBASE, 28 using MEDLINE, 98 using Pubmed, and 8 using CINAHL, totalling 178 articles of which 66 were selected to be examined further. Following removal of duplicate search results, this left 37 articles to be reviewed in full.

Of these, 6 met all the inclusion criteria and were included in the final literature review. These articles were used to assess both current knowledge about the effects of a combination of solvents found in JP-8 and noise on central auditory function, and to identify potential recommendations for filling the gaps in the literature. Table I summarizes the studies discussed in this review.

Study Characteristics

Of the 37 articles reviewed in full, 2 were prospective case-control studies, 19 were retrospective case-control studies, 2 were cross-sectional studies, 5 were review articles, 2 were conference proceedings, 3 were opinion/perspective articles, and 4 were case studies. When identifying which articles to include in this review, the most common reasons for rejection were that they used animal models, examined a solvent that was not a component of jet fuel (e.g., styrene), and the conference proceedings were not detailed enough to be critically analyzed.

REVIEW

Studies Investigating Subjects Exposed to Jet Fuels and Noise

Kaufman et al¹⁴ sought to examine the effects of occupational exposure to jet fuel and noise on hearing in military aircraft maintenance workers. One hundred and thirty eight noise-exposed subjects, all of whom were required to have a minimum of 3 years of occupational noise exposure (85 dBA or greater), with or without jet fuel exposure (estimated as 0 to 33% of annual cumulative exposure based on threshold limit values/permmissible exposure limit (TLV/PEL) of 700 mg/m³ = 161,000 mg/m³ per year), underwent pure-tone audiometry. Work histories, recreational exposures, protective equipment, medical histories, alcohol, smoking, and demographics were collected by questionnaire. JP-4 jet fuel, solvents (benzene, toluene, xylene, hexane, and heptane), and noise exposure data were collected from records.

Kaufman's findings suggested that jet fuel has a toxic effect on the auditory system. Noise, tinnitus, and age were also found to be significant factors in persistent hearing loss. Duration of jet fuel exposure increased the odds of persistent hearing loss even though the estimated exposures were well below the TLV and PEL. Fuel exposure estimates were less than 34% of the Occupational Safety and Health

TABLE I. Summary of Reviewed Articles

Author	N° Subjects	Solvent	Noise	Measurements	Effectuated Systems	Results
Kaufman et al (2005)	138	JP-4 Jet Fuel	>85 dBA	Hearing Thresholds	Peripheral Auditory System	Increasing Odds of PHL with Increasing Duration of Jet Fuel, and Jet Fuel and Noise Exposure
Prasher et al (2005)	379	Benzene, Toluene, Xylenes, Naphthalene, Trichloroethane, Dimethylacetamide, <i>n</i> -hexane, etc.	>85 dBA	Tympanometry, Acoustic Reflexes, DPOAE, TEOAE, ABR, Nystagometry, Posturography	Peripheral and Central Auditory Systems	Significant Effect on PTA, DPOAE, and TEOAE Abnormalities, ABR Abnormalities, Abnormal Nystagometry and Posturography
Gopal (2008)	7	Toluene, Xylene	>85 dBA	Case History, Otoscopy, PTA, OAE, SCAN-A, R-SPIN, ABR, MLR	Peripheral and Central Auditory Systems	Abnormal Retrocochlear/CANS Findings, Abnormal ABR, Difficulty in Auditory Processing
Fuente and McPherson (2006)	20	Toluene, Xylene, Methyl Ethyl Ketone	<85 dBA	PTA, Acoustic Reflexes, DD, PPS, MLD, FS, RGD, HINT	Peripheral and Central Auditory Systems	Normal Hearing Thresholds, Reduced Performance on Behavioural Measures
Fuente et al (2007)	60	Solvents (Mixed)	<85 dBA	PTA, FS, RGD, HINT	Peripheral and Central Auditory Systems	Normal Hearing Thresholds, Reduced Performance on Behavioural Measures
Fuente et al (2009)	110	Toluene, Methyl Ethyl Ketone (+ Others)	<85 dBA	PTA, HFA, DD	Peripheral and Central Auditory Systems	Normal Hearing Thresholds, Reduced Performance on Behavioural Measures

PHL, persistent hearing loss; PTA, pure-tone audiometry; OAE, otoacoustic emissions; ABR, auditory brainstem response; MLR, mid latency response; BAEP, brain auditory evoked potentials; DD, dichotic digits; PPS, pitch pattern sequence; MLD, masking level difference; FS, filtered speech; RGD, random gap detection; HINT, hearing in noise test; HFA, high-frequency audiometry; R-SPIN, revised speech perception in noise.

Administration TLV. Subjects with 3 years of jet fuel exposure had a 70% increase in adjusted odds of hearing loss and the odds increased to 2.41 for 12 years of noise and fuel exposure.

Kauffman used only pure-tone audiometry to investigate the auditory system (hearing threshold loss), there were no behavioral or electrophysiological tests administered which could have specifically led to evaluation of the CANS. In addition, jet fuel, solvent, and noise exposure data were collected from records, but there were no contemporary measurements taken at the time of evaluation. Kaufman's cross-sectional investigation of 2005 was the first study of potential neurotoxicity of jet fuel exposure. As pure-tone audiometry was used, it is not possible to conclude whether the effect would relate to oto- or neurotoxicity. This investigation predominantly examined the effects of JP-4 because JP-8 was introduced to the military installation less than 2 years previous to the study. JP-8 contains lower percentages of known ototoxins such as toluene and xylene than JP-4, but evaporates more slowly, creating an increased opportunity for dermal absorption.

In summary, exposure estimates in aircraft maintenance workers were well below the TLV. Despite the low levels of fuel exposure, statistically significant increases in the probability of a persistent hearing loss were observed in noise and jet fuel-exposed subjects.

Studies Investigating Subjects Exposed to Aromatic Solvent Components of JP-8 and Noise

Prasher et al¹⁵ investigated aircraft maintenance workers exposed to a complex mixture of solvents, including benzene, *n*-hexane, toluene, xylenes, naphthalene, trichloroethane, and dimethylacetamide, in the presence of intermittent noise (*n* = 174) and compared them to control groups of noise only (*n* = 153), solvents only (*n* = 13), and no exposure (*n* = 39). The members of the control groups were not aircraft maintenance personnel (mill workers exposed to noise alone, printed circuit board operatives exposed to solvents only) and the authors did not identify the non-exposed group other than they had no exposure to either solvents or noise. Tympanometry, acoustic reflex thresholds, transient evoked otoacoustic emissions and distortion product otoacoustic emissions, ABR, nystagometry, and posturography were examined.

Measurements of the noise level were taken from aircraft maintenance workers on 9 occasions over 3 days over a period of a year. Both LA_{eq} (59.6–97.9 dB) and LA_{peak} (84.9–115.9 dB) levels, including levels over the spectral range were recorded. No data was provided for the noise only group; however, the authors stated that the major difference in the noise exposure between the two groups was the fact that the aircraft maintenance workers were exposed to a wide range of levels with relative quiet periods, whereas the noise alone group were in constant noise during their work time.

Although the authors stated that solvent exposure in the relevant groups was estimated from years of work and the type of work undertaken in that time and that it was not possible to take urine or blood measurements of the workers, no data was provided.

There was a significant effect on pure-tone thresholds for both the noise+solvents and noise groups. The distortion product otoacoustic emissions declined with frequency and exhibited lower amplitude with noise compared to the noise+solvents group. The transient evoked otoacoustic emissions showed a similar effect. Over 32% of subjects with noise+solvents exposure had abnormalities of the ABR in terms of interwave interval prolongation of intervals I to V. ABR abnormalities in the noise+solvents group also indicated that the central auditory pathway was affected in this group. This is in agreement with a study of airport employees by Chen et al¹⁶ (which was excluded from this review as it was before 1993) who reported prolongation in central conduction time in ABR intervals I to V and III to V.

The mean acoustic reflex thresholds showed a pattern of differences which differentiate the noise only group from the noise+solvents group. The correlation between ipsilateral and contralateral reflex thresholds for the right ear and left ear were significant for almost all frequencies for the control and noise groups, but not significant for the left ear for the noise+solvents group. This significant observation shows an absence of any increase in reflex thresholds contralaterally for the noise+solvents group. Normally, there is 5 to 7 dB increase in contralateral reflex threshold,¹⁵ which was absent in the noise+solvents group. As there were no differences in the ipsilateral reflex thresholds across groups, the lower contralateral reflex thresholds in the noise+solvents groups were the key difference between groups. The contralateral pathway appears to be differentially affected by solvent exposure. The number of subjects in the noise+solvents group that had an absent reflex ipsilaterally was 25.1% compared with 41.2% contralaterally but this was not statistically significant.

Another interesting finding was that the correlation between ipsilateral and contralateral reflexes in the control and noise groups was highly significant especially for the left ear but was not at all significant for the noise+solvents group especially for the left ear. These findings of altered contralateral reflexes imply an effect of solvents on the central crossed auditory pathway as no deficiencies were observed in the noise alone group or the controls.

The effect of solvent exposure on the CANS is further supported by abnormalities of the ABR in the noise+solvents group. In this group, prolongation of central conduction time for the ABR waves I to V interval, presence of waves I and III in the absence of wave V, and unreproducible responses were observed, although no significant differences in the mean latencies of the waves were noted across groups.

There were a number of limitations in this study, which meant that only limited conclusions could be drawn. The study groups were unmatched in terms of numbers in each group

and, because of time constraints, the researchers were unable to identify a match for noise exposure level between the noise only and noise+solvents group. The study did make a number of valid observations, many of which were in agreement with Chen and Chen's findings of 1992,¹⁶ though they should be considered with caution. The Chens' work demonstrated that the results of audiometry and ABR were closely coincident with job patterns, and the ABR results, in particular, suggested involvement of the central auditory pathway.

A study by Gopal¹⁷ reported results from seven adults who (self reportedly) had a history of exposure to toluene, xylene, or both, for a period of at least 3 years, and six out of seven individuals had a history of exposure to noise, although the level of noise was not identified. All were put through a test battery consisting of: case history, otoscopy, pure-tone audiometry, otoacoustic emissions, behavioral and electrophysiological tests investigating the CANS.

In this study, abnormal retrocochlear/central findings were identified in one or more auditory test measures among all solvent exposed individuals. Furthermore, some of these subjects had normal pure-tone hearing thresholds, but revealed poor speech processing scores, elevated or absent acoustic reflex thresholds, and abnormal auditory evoked potential test results. These findings suggest central auditory involvement from possible exposure to solvents.

Six out of seven subjects in this investigation showed abnormal acoustic reflex thresholds (elevated or absent) with ipsilateral and/or contralateral stimulation despite normal pure-tone thresholds at the corresponding frequencies. All subjects in this study revealed normal tympanograms, thus ruling out middle ear disorders. In the presence of normal thresholds and absence of conductive impairment, abnormal acoustic reflex thresholds (ipsilateral or contralateral) are considered uncharacteristic, suggesting central auditory dysfunction.¹⁷

Gopal's study also showed poor or abnormal scores when the CANS were examined with behavioral tests. In this study, poor or abnormal Test for Auditory Processing Disorders in Adolescents and Adults (SCAN-A) scores were found in 4 subjects. An abnormal score on the SCAN-A indicates that the subject is at risk for central auditory processing disorder.¹⁸ Based on the normative data set,¹⁸ four subjects were found to exhibit abnormally low scores. These findings, indicating difficulty in processing auditory signals, are comparable to the findings of Fuente et al¹⁹ who found statistically significant differences in central auditory processing abilities between workers who had been exposed to a mixture of solvents which contained toluene, xylene, and methylethylketone (with noise levels below 85 dBA) and non-exposed control workers.

Gopal also found that ABR waveforms were abnormal in four subjects, as were mid-latency response (MLR) measures. It is important to note that all seven subjects with solvent exposure, whether exposed to noise or not, showed aberrations of ABR measures, MLR measures, or both. ABR and MLR are widely used in the objective evaluation of the performance of the auditory pathway from the auditory nerve to

the auditory cortex.¹⁷ Abnormalities of absolute latency, inter-peak latency, amplitude, amplitude growth measures, and waveform morphology (noisy, poor repeatability, shallow, or less sharply peaked responses) are considered as indicators of aberration of the auditory nerve, brainstem, thalamus, or the cortex.¹⁷ In this study, the ABR waveforms were abnormal in 4 subjects, as were MLR measures.

All seven individuals examined in this study had some degree of retrocochlear and/or central auditory abnormalities. The combined test battery approach (psychoacoustic and electrophysiological measures) used here appears to be useful in evaluating the pathological conditions of the CANS in solvent exposed individuals and seems to be sensitive for the identification of retrocochlear and central abnormalities.

Fuente has undertaken a number of studies investigating the effects of solvents on central auditory function.^{19–22} Although noise was also considered, not all subjects were exposed to high levels of noise.

In a 2006 study,¹⁹ 10 workers occupationally exposed to a mixture of organic solvents containing toluene, xylene, and *n*-hexane and low levels of noise (<85 dBA); and 10 matched non-exposed workers were studied for central auditory processing abilities. The test battery comprised pure-tone audiometry, tympanometry, acoustic reflex measurement, acoustic reflex decay, dichotic digit (DD), pitch pattern sequence (PPS), masking level difference (MLD), filtered speech (FS), random gap detection (RGD), and hearing-in-noise (HINT) tests. All the workers presented normal hearing thresholds and no signs of middle ear abnormalities. Workers exposed to solvents had lower results in comparison with the control group and previously reported normative data in the majority of the tests.

A second study in 2007²⁰ investigated possible central auditory processing disorders related to solvent exposure in 30 solvent-exposed workers (workers in a paint factory) and 30 gender-, age-, and educational level-matched control subjects. The specific solvents the painters were exposed to were not identified in the article; however, the most widely used solvents in paint are benzene, toluene, xylene, ethylbenzene, high flash aromatic naphthas and aliphatic hydrocarbons—the same solvents found in jet fuel. Exposure to noise over 85 dB was an exclusion criterion, though there would have been some level of noise exposure in a factory. Again, a questionnaire, otoscopy, pure-tone audiometry and tympanometry, FS, RGD, and HINT procedures were conducted. Both groups of workers presented with mean normal hearing thresholds. However, significant differences between groups were observed for RGD, FS, and HINT. It was concluded that a possible central auditory processing disorder may be related to solvent exposure.

In 2009, Fuente et al²² examined the effects of solvent exposure (toluene, methylethylketone, trichloroethylene, acetone, *n*-methyl pyrrolidone, dimethylformamide, chlorobenzene, and isopropyl alcohol were known to be used in the factory) on hearing function, through an audiological test

battery, in a population not occupationally exposed to high levels of noise (documented noise levels in the plant ranged from 74 to 84 dBA). One hundred and ten workers from a coating factory were studied. Jobs at the factory were divided into three different levels of solvent exposure. Hearing status was assessed with a test battery including pure-tone hearing thresholds (0.5–8 kHz), high-frequency hearing thresholds (12 and 16 kHz), and dichotic listening measured through DD test. Significant associations between solvent exposure and the three hearing outcomes were found. Covariates such as age, gender, race, and ethnicity were also significantly associated with the studied hearing outcomes. Given the likely exposures in a coating factory, lead exposure may have been a confounder, but there was no mention of blood lead levels or lead exposure being measured in this study.

These three studies suggest that occupational exposure to organic solvent mixtures has an adverse effect on central auditory function assessed by behavioral means. These findings lead to a hypothesis that solvents induce a subtle central auditory dysfunction at early stages, as observed by dichotic listening.²²

CONCLUSION

The results of the literature review suggest that there is an association between aromatic solvents, including jet fuel, in combination with noise and central auditory dysfunction/hearing loss. Field studies have shown an association between exposure to aromatic solvents such as jet fuel and effects in the central auditory pathway. However, the paucity of evaluative studies and disparate findings in those that have been conducted, along with variations in study design, provide only a partial understanding of occupational exposure to jet fuel and noise on the CANS in military aviation maintenance workers. Given the high rate of hearing-related disabilities in the Australian Defence Force and Australian veteran community, additional studies are greatly needed to assess the effects of combined exposures to jet fuel and noise on the CANS in the Australian Defence Force, and other militaries worldwide.

Ideally, future studies will use behavioral and electrophysiological tests to provide the most comprehensive assessment of the CANS. The studies should assess multiple time points—the test battery being administered both before and after periods away from exposure, e.g., periods of leave, to identify chronic and acute symptoms resulting from the exposure. It would also be beneficial to conduct environmental screening such as noise and solvent levels in the workplaces of the study participants to verify and quantify exposure, as well as dose response relationships. Urinalysis of relevant biomarkers would also add an additional measure of exposure to solvents and jet fuel. Such a study, incorporating all of these aspects, is currently underway at the University of Queensland, Australia.

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