# Audiological Tests Used in the Evaluation of the Effects of Solvents on the Human Auditory System: A Mixed Methods Review

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## ABSTRACT

This study aimed to scope the literature, identify knowledge gaps, appraise results, and synthesize the evidence on the audiological evaluation of workers exposed to solvents. We searched Medline, PubMed, Embase, CINAHL, and NIOSHTIC-2 up to March 22, 2021. Using Covidence, two authors independently assessed study eligibility, risk of bias, and extracted data. National Institute of Health Quality Assessment Tools was used in the quality evaluation of included studies; the Downs and Black checklist was used to assess the risk of bias. Of 454 located references, 37 were included. Twenty-five tests were studied: two tests to measure hearing thresholds, one test to measure word recognition in quiet, six electroacoustic procedures, four electrophysiological tests, and twelve behavioral tests to assess auditory processing skills. Two studies used the Amsterdam Inventory for Auditory Disability and Handicap. The quality of individual studies was mostly considered moderate, but the overall quality of evidence was considered low. The discrepancies between studies and differences in the methodologies/outcomes prevent recommending a specific test battery to assess the auditory effects of occupational

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The National Institute for Occupational Safety and Health: Occupational Hearing Loss; Guest Editors, Elizabeth A. Masterson, Ph.D., CPH, COHC and William J. Murphy, Ph.D., M.S., M.Eng.

Semin Hear 2023;44:437–469. 
Thieme Medical Publishers, Inc., 333 Seventh Avenue, 18th Floor, New York, NY 10001, USA
DOI: https://doi.org/10.1055/s-0043-1769585.
ISSN 0734-0451.

solvents. Decisions on audiological tests for patients with a history of solvent exposures require the integration of the most current research evidence with clinical expertise and stakeholder perspectives.

**KEYWORDS:** solvents, ototoxicity, work-related hearing loss, scoping review

The observed effects of workplace chemical exposures, such as toluene, styrene, and xylene, on the auditory system, are diverse. This variety of negative auditory outcomes has motivated the use of different audiological test batteries.[1–6] Cases of audiometric hearing loss induced by chemicals have been reported to range from mild to moderate. The high-frequency audiometric notch commonly seen in noise-induced hearing loss (NIHL) is also often present after prolonged exposure to chemicals, although some reports indicate that broader frequency bands are affected when compared to those affected by noise exposures alone (for details from specific studies, see Johnson and Morata, 2010).[1] It should be emphasized, however, that ototoxic chemicals do not always significantly affect audiometric thresholds.

Many studies have shown that some chemicals may affect not only the sensory organ of the auditory system (the cochlea) but also may lead to adverse effects on the central auditory structures.[7–10] Clinical studies have suggested that exposure to certain industrial chemicals may have retrocochlear effects.[11,12] Chemicals such as organic solvents, metals, and asphyxiants are known for their neurotoxic effects on both the central and peripheral nervous system[1,6] and in addition they can modify the effects of noise.[9,13] Chemicals such as solvents, pesticides, and metals have neurotoxic properties that can damage to the brain as well as sensory and/or neural elements of the ear.[5,7,14] Signs of neurotoxicity in the auditory system may or may not include poor auditory thresholds, but they relate to difficulties in discriminating sounds, such as speech, mainly in adverse listening conditions.[6,7]

Among the chemicals found in the workplace with potential adverse effects for the auditory system, solvents are the most studied. Millions of people around the world are exposed to organic solvents such as toluene and xylene in the manufacturing sector alone.[5,15,16]

Taking into consideration that neurotoxic effects of solvents can impact many different biological pathways and structures important to processing sound in both the ear and the brain, the use of a battery of tests has been proposed.[17–21] However, there is still no clear consensus about which tests should be included in this battery. Thus, the objective of this mixed methods review was to scope the body of literature, identify knowledge gaps, appraise findings, and synthesize the evidence in total on the audiological assessment of workers exposed to solvents. This comprehensive review should aid audiologists and other health care professionals in their decision making when determining the full extent of auditory damage and providing treatment for this population.

## METHODS

This mixed methods review combined the framework of a scoping review, which delineates the coverage and focus of a body of literature with an evidence synthesis[22] and key features of a systematic review. These include framing the question in a structured and explicit way; using a comprehensive, transparent, and reproducible search of the literature; and conducting the quality assessment of included studies.[23] A scoping review also allows the identification of the nature of a broad field of evidence and evaluates if a systematic review or meta-analyses are feasible.

The search strategy was performed in five electronic databases: Medline (OVID), PubMed, Embase (OVID), CINAHL, and NIOSHTIC-2. The search was set to include all English, Spanish, Portuguese, or Italian language studies (restricted to humans), no time restriction up to March 22, 2021. Citations were imported into EndNote where duplicates were removed. Remaining search results were uploaded into Covidence for the completion of the next steps. All studies directly involving the audiological tests among workers exposed to solvents were reviewed independently by two authors and selected for further analysis. Discrepancies between reviewers were resolved by discussion. To avoid conflicts of interest, none of the co-authors of this manuscript analyzed their own studies eligibility or quality during the review process.

## ELIGIBILITY CRITERIA

A population, exposure, comparator, and outcomes (PECO)[24] statement guided eligibility decisions. Inclusion criteria required the study population to consist of workers exposed to solvents in the workplace (regardless of their noise exposure) who received audiological testing not restricted to pure-tone audiometry (studies which only reported pure-tone audiometry results were excluded). Given that the focus of the present review was audiological clinical tests exploring the auditory system, studies involving only balance and neurobehavioral findings were also not included. The auditory testing results from exposed workers had to be compared to results from a control population who were not exposed to these agents. The use of standardized questionnaires to explore effects of solvent exposure on hearing were considered as a complement to audiometry and thus eligible for inclusion. Studies had to have a control group to be included; so, studies which compared only results with normative criteria were excluded. Studies were evaluated in three stages: (1) title and abstract screening, (2) full-text review, and (3) data extraction in combination with quality assessment.

## DATA EXTRACTION AND ASSESSMENT OF RISK OF BIAS IN INCLUDED STUDIES

After identifying studies meeting all inclusion criteria, the following data were extracted from each article by two independent reviewers: publication year, study design, sample size, study purpose, target population (e.g., age, gender, job category, and industry), as well as audiological tests used and other reported outcomes. To judge the quality of each article, as demonstrated by internal validity, we used the Downs and Black[25] checklist and two tools from the National Institute of Health: (1) the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies and (2) the Quality Assessment of Case-Control Studies.[26] The domains used for the quality evaluation of study designs included: clarity of the research question, study population, uniformity of eligibility criteria among sub-groups, statistical power, exposure assessment information, levels of exposures, allowing a sufficient time frame to see an effect, methods for measuring outcomes, blinding of outcome assessors, follow-up rate, and statistical analysis. For this review, data extractions and quality assessments were accomplished by two different review authors working separately. Review authors did not participate in eligibility or quality assessment decisions of articles they had authored. Any disagreements within quality assessment findings were resolved through discussion between the two evaluators.

## RESULTS

The search yielded 454 references in total. The screening of abstracts and titles for inclusion eligibility by pairs of review authors resulted in 73 articles which were retrieved in full text; one study was located when we scanned the reference lists of identified studies for further articles. Thirty-seven studies fulfilled the eligibility criteria (see Fig. 1). Thirty of them are cross-sectional studies, defined as those which determined participant selection by exposure. Seven case–control study designs were included, defined as studies which compared workers who were suspected to have or already diagnosed with a health outcome, for example, psycho-organic syndrome or chronic encephalopathy (however, these case–control studies could also be considered cross-sectional, as they do not investigate exposure frequencies which a formal case–control study definition requires). All studies compared hearing outcomes in workers across one or more exposure groups to a control group with no solvent exposures. Participants in all studies were described as exposed to solvents

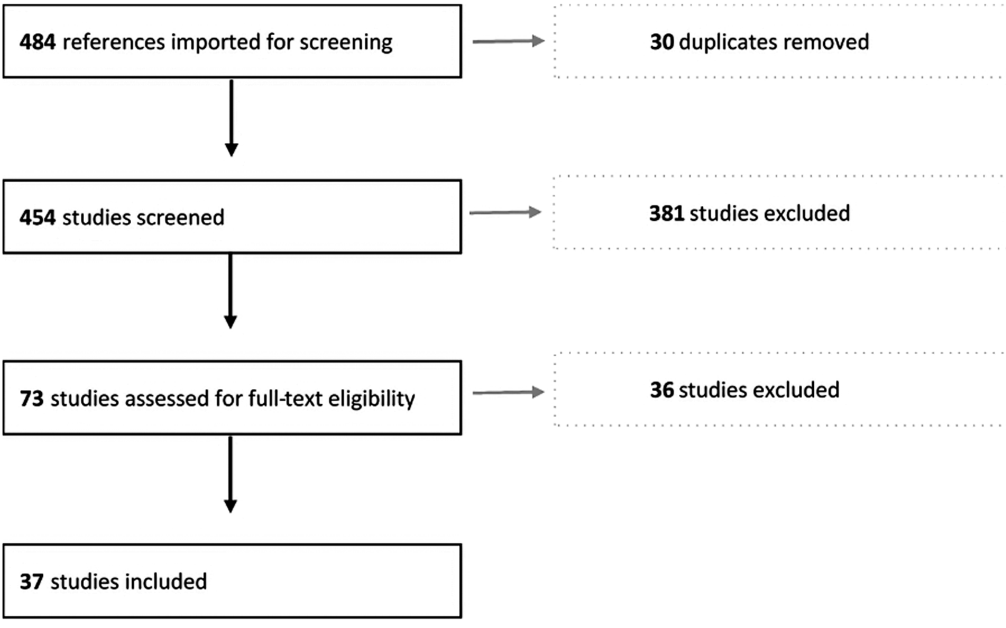


**Figure 1** Prisma study flow diagram for this review ultimately including 37 studies.

at work, some individual (e.g., styrene or chlorinated hydrocarbons), some in mixtures, and some in combination with noise exposures. However, workplace exposure descriptions were often based on sporadic measurement methods or not clearly described. Most studies included only men as there was a majority of male workers in workplaces that were studied. A description of study designs, auditory testing results, and system affected/conclusions for the 37 included studies can be seen in Appendix Table A1. Technical descriptions of the tests used in the studies can also be found in previous publications.[1]

## RISK OF BIAS IN THE INCLUDED STUDIES

The authors' judgments about each risk of bias item for each included study were guided by the Downs and Black checklist.[25] An overview of checklist results is shown in Figs. 2 and 3. The review authors' judgments about each risk of bias item (presented as percentages across all included studies in Fig. 2) indicate low risk of bias in several categories of the individual criterion of the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.[26] The risk of bias analysis is unclear for important criteria such as "participation rate," "outcome analysis by different exposure parameters," and "assessors blinding." In addition, the overall quality of evidence was considered low because of their design, given that all included studies were either cross-sectional studies or case–control.

## Outcomes and Measures

The present review focused on audiological tests that were used to examine workers exposed to solvents, often to complement pure-tone audiometric findings. Fourteen studies that evaluated only pure-tone audiometry results were not included. Twelve of those studies report higher prevalence rates of hearing loss associated with solvent exposure. The audiological tests used in the included studies, as well as the auditory aspects and the structures of the system evaluated by each test, and the total number of articles that used each one of the auditory tests can be observed in Table 1.

A total of 25 different auditory tests were used to evaluate the auditory system of workers exposed to solvents. These included two different types of behavioral tests to measure hearing

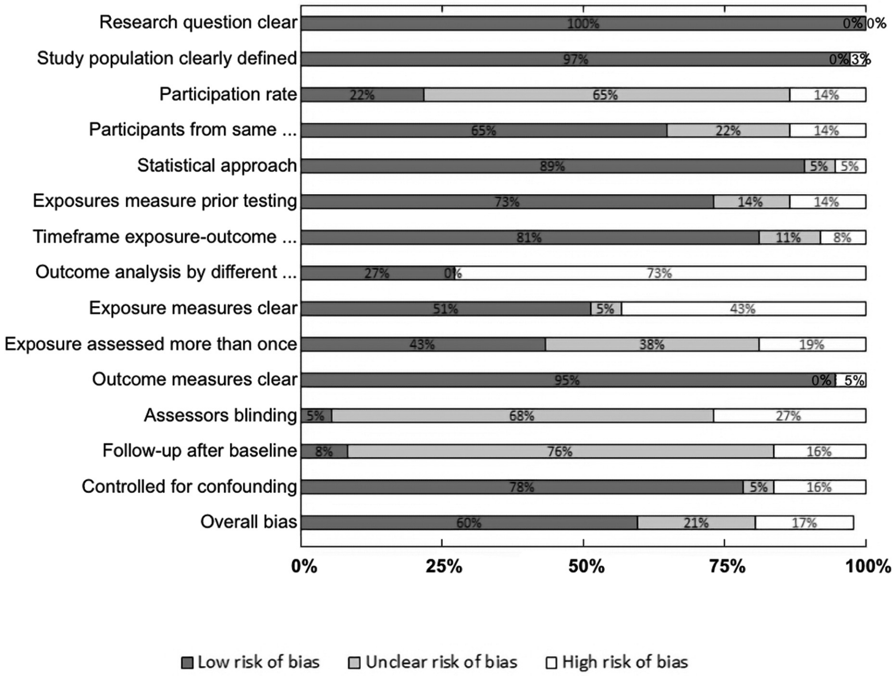


**Figure 2** Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies.

thresholds, one behavioral test to measure word recognition in quiet, six different electroacoustic procedures, four different types of electrophysiological tests, and 12 different behavioral tests used to assess auditory processing skills. In addition, two studies used the Amsterdam Inventory for Auditory Disability and Handicap (AIADH) which is a self-report questionnaire. Pure-tone audiometry was the most used auditory test (25 studies), and auditory brainstem response (ABR) was the second most used test (15 studies). Tables 2 to 5 identify the auditory tests, sorted by test category, which have reported significant differences between solvent-exposed and unexposed participants. Several of the included studies report only *p*-values of the comparisons between study groups and do not report effect sizes. While we included p-values when reported by the authors of the included studies we alert readers that such values are arbitrary. Nonstatistically significant results should not be dismissed as they may conceal potentially important public health effects.[27]

Statistical differences between exposed and unexposed groups in pure-tone thresholds were reported only in less than half of the studies in which it was used (12 of 25 studies). As can be seen in Appendix Table A1, all these studies showed poorer hearing thresholds in workers exposed to solvents than in those not exposed, and in four of these studies,[16,20,28,29] differences were found even with all hearing thresholds within the normal range in both groups. The second most utilized testing methodology of the 37 studies reviewed was ABR shown in Table 4.

In Tables 2 to 5, the following tests showed statistically significant differences between solvent-exposed and solvent-unexposed participants in all studies in which they were used: AIADH (two studies), Transient-Evoked Otoacoustic Emission (TEOAE) contralateral suppression (one study), Dichotic Digit (DD) test (five studies), Filtered Speech (FS) test (four studies), Hearing-in-Noise Test (HINT; six studies), Swedish Speech Recognition in Noise (one study), Pitch Pattern

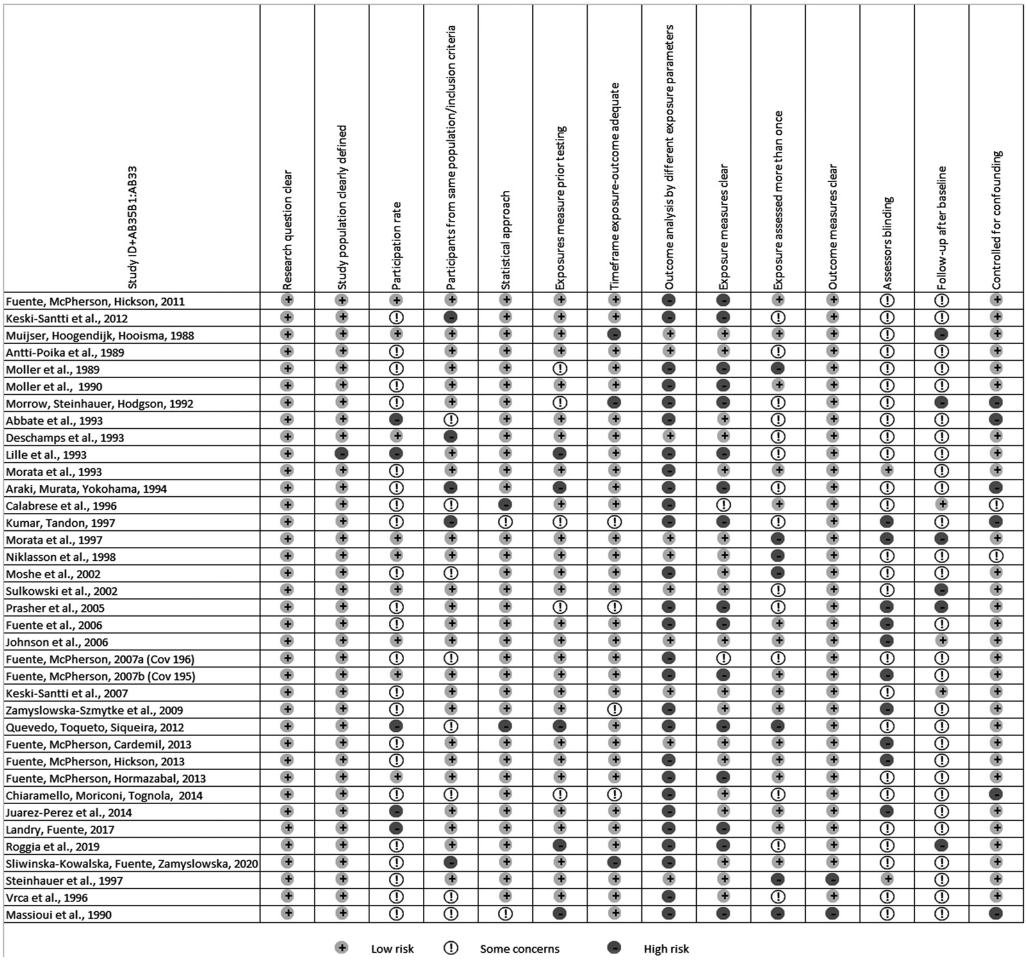


**Figure 3** Risk of bias summary: review authors' judgments about each risk of bias item for each included study.

Sequence (PPS) test (five studies), Random Gap Detection (RGD) test (six studies), Duration Pattern Sequence (DPS) test (one study), and Psychoacoustical Modulation Transfer Function (PMTF) test (one study). In addition, the following tests showed statistically significant differences between participants exposed and unexposed to solvents in half or more of the studies: acoustic reflex decay (two of three studies), TEOAE (four of six studies), DPOAE (three of six studies), and P300 (four of seven studies). The following tests did not show significant differences between solvent-exposed and solvent-unexposed participants in any study where they were used: Adaptive Tests of Temporal Resolution (ATTR; one study), Gaps in Noise (one study), and Masking Level Difference (MLD) test (three studies).

Abnormal clinical results were found in several tests used, as can be seen in Appendix Table A1. Considering both statistical differences between exposed and unexposed participants, as well as the presence of clinically abnormal results in the applied tests, only two of the included studies did not test and consequently could not have shown impairment in the central auditory nervous system (CANS).[30,31] Several studies concluded that solvents may trigger central auditory dysfunction even when participants have normal-hearing audiometric thresholds.[16,20,28,29] Thirteen studies which tested auditory performance in the peripheral auditory system did not find an

**Table 1 Types of auditory tests used in 37 epidemiological studies on solvent ototoxicity included in this review**

| Type of test | Test name | Auditory aspect or structure evaluated | Number of studies | References |
|---|---|---|---|---|
| Self-report questionnaire | Amsterdam Inventory for Auditory Disability and Handicap | Subject's self-perception of performance in real-life listening situations; functional assessment of hearing ability | 2 | 28,29 |
| Behavioral | Pure-tone audiometry | Hearing thresholds (250–8,000 Hz) | 25 | 8,16,20,28–38,55,56,59–63,68,69,75,80 |
| | Extended high-frequency audiometry | Hearing thresholds (9,000–20,000 Hz) | 3 | 30,55,56 |
| | Word recognition in quiet | Speech perception in quiet | 3 | 32,33,35 |
| Electroacoustic | Acoustic reflex thresholds | Acoustic reflex pathway | 6 | 34,59–63 |
| | Acoustic reflex decay | Adaptation of the acoustic reflex | 3 | 37,59,61 |
| | Spontaneous otoacoustic emissions | Outer hair cell function | 1 | 63 |
| | Transient-Evoked Otoacoustic Emission (TEOAE) | Outer hair cell function | 6 | 16,31,39,60,62,63 |
| | Contralateral suppression of TEOAE | Medial olivocochlear system | 1 | 39 |
| | Distortion Product Otoacoustic Emissions | Outer hair cell function | 6 | 56,60,62,63,68,69 |
| Electrophysiological | Auditory Brainstem Response | Neural synchrony of the auditory nerve fibers and auditory structures of the brainstem | 15 | 34,36,40–43,54–56,60,62,69,73–75 |
| | Cortical Response Audiometry[a] | Electrophysiological activity of auditory areas in the cortex | 4 | 32,33,35,68 |
| | Late Auditory Evoked Potentials[b] | Electrophysiological activity of auditory areas in the cortex | 3 | 44,45,73 |
| | P300 | Electrophysiological activity triggered by the discrimination of acoustic features through the use of an oddball paradigm | 7 | 42,44–47,60,73 |
| Behavioral tests used to examine auditory processing skills | Adaptive Tests of Temporal Resolution | Temporal resolution | 1 | 69 |
| | Dichotic Digit test | Binaural integration and separation | 5 | 8,20,28,37,69 |
| | Duration Pattern test | Temporal processing. Discrimination of sound duration, temporal ordering, and sequencing | 1 | 80 |

(*Continued*)

**Table 1 (*Continued*)**

| Type of test | Test name | Auditory aspect or structure evaluated | Number of studies | References |
|---|---|---|---|---|
| | Filtered Speech | Auditory closure | 4 | 20,28,37,38 |
| | Gaps in Noise Test | Temporal resolution | 1 | 80 |
| | Hearing in Noise Test | Sound segregation, auditory closure | 6 | 16,20,28,37,38,69 |
| | Interrupted Speech | Auditory closure | 4 | 32,33,35,68 |
| | Masking Level Difference | Binaural interaction | 3 | 20,37,69 |
| | Pitch Pattern Sequence | Temporal processing. Discrimination of sound frequency; temporal ordering and sequencing | 5 | 20,28,37,69,80 |
| | Psychoacoustical Modulation Transfer Function | Tone detection in the presence of fluctuating noise. Sound segregation | 1 | 68 |
| | Random Gap Detection test | Temporal resolution | 6 | 16,20,28,29,37,38 |
| | Speech Recognition in Noise | Sound segregation, auditory closure | 1 | 68 |

[a]Cortical response audiometry (CRA): all studies were included in which the authors named the test as CRA, and the evoked-related potential (ERP) components were not specified in the articles.
[b]Late auditory evoked potentials (LAEP): included those studies with one or more of the following components: N1, N100, N2, N200, N250, P1, P2.

adverse effect of solvent exposure on peripheral auditory structures as measured by the following methodologies: pure-tone audiometry,[8,32–38] acoustic reflex threshold (ART),[34] TEOAE,[39] and ABR.[34,36,40–43] Four of the reviewed studies did not include testing for peripheral auditory dysfunctions.[44–47]

Overall, many different tests have been used across the 37 included studies to determine the adverse effects from solvent exposure on the human auditory system. Differences in study methodologies, exposure scenarios, and various levels of inconsistency in study findings make it difficult to determine with precision what hearing tests should be included in a test battery for populations exposed to ototoxicants in the workplace. However, this review elucidates the type of auditory dysfunctions to be expected, which can inform the selection of diagnostic tests to use with this population.

## DISCUSSION

### Self-Report Listening Questionnaire

Only two studies in this review used a self-report questionnaire about listening performance.[28,29] Both of these studies used the Amsterdam Inventory for Auditory Disability and Handicap.[48] Both found that workers exposed to solvents presented with significantly more listening difficulties in daily-life activities than unexposed participants. Specifically, Fuente et al[29] found that workers exposed to solvents from two paint-making factories reported poorer listening performance for sound detection (peripheral auditory function), speech discrimination (central auditory function), and sound localization/lateralization (central auditory function) than participants not exposed to solvents. In addition, the authors determined the AIADH scores were significantly associated with pure-tone thresholds and RGD results. A recent study by Dreisbach et al[49] reported consistent and marked lower scores of a modified AIADH version for a group of military personnel exposed to jet-fuels, when compared to a control group.

The use of a self-report questionnaire about listening performance in daily-life activities such as the AIADH can be useful to detect the functional impact of the effects of solvent

**Table 2 Statistical differences between solvent-exposed and nonexposed workers of audiological outcomes for 25 epidemiological studies: self-report questionnaires and behavioral auditory tests**

| Study | AIADH | | | PTA | | | EHFA | | | WR | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | NSD | SIG | NR | NSD | SIG | NR | NSD | SIG | NR | NSD | SIG | NR |
| Muijser et al[30] | | | | x | | | x | | | | | |
| Antti-Poika et al[75] | | | | | | x | | | | | | |
| Möller et al[32] | | | | | | x | | | | | | x |
| Möller et al[33] | | | | | | x | | | | | | x |
| Morata et al[59] | | | | | x | | | | | | | |
| Calabrese et al[34] | | | | | | x | | | | | | |
| Morata et al[61] | | | | | x | | | | | | | |
| Niklasson et al[35] | | | | x | | | | | | | | x |
| Moshe et al[36] | | | | x | | | | | | | | |
| Sułkowski et al[63] | | | | | | x | | | | | | |
| Prasher et al[62] | | | | | | x | | | | | | |
| Fuente et al[37] | | | | x | | | | | | | | |
| Johnson et al[68] | | | | | x | | | | | | | |
| Fuente and McPherson[38] | | | | | | x | | | | | | |
| Fuente and McPherson[28] | | x | | | x | | | | | | | |
| Zamyslowska-Szmytke et al[80] | | | | | x | | | | | | | |
| Fuente et al[20] | | | | | x | | | | | | | |
| Fuente et al[69] | | | | | x | | | | | | | |
| Fuente et al[16] | | | | | x | | | | | | | |
| Fuente et al[29] | | x | | | x | | | | | | | |
| Chiaramello et al[31] | | | | | | x | | | | | | |
| Juárez-Pérez et al[55] | | | | | x | | | | x | | | |
| Landry and Fuente[8] | | | | x | | | | | | | | |
| Roggia et al[60] | | | | | x | | | | | | | |
| Sliwinska-Kowalska et al[56] | | | | | x | | | x | | | | |
| Total | 0/2 | 2/2 | 0/2 | 5/25 | 12/25 | 8/25 | 1/3 | 1/3 | 1/3 | 0/3 | 0/3 | 3/3 |

Abbreviations: NSD, no statistical difference; SIG, statistically significant difference; NR, not reported (included all studies where the authors did not report test results, or if they did not mention whether there was a statistical difference between the groups); AIADH, Amsterdam Inventory for Auditory Disability and Handicap; PTA, pure-tone audiometry; EHFA, extended high-frequency audiometry; WR, word recognition in quiet (this also includes maximum discrimination speech, speech discrimination, speech recognition).

exposure on the auditory system. Inventories, such as the AIADH, explore hearing functions that go beyond sound detection thereby investigating performance of aspects associated with both the peripheral and central auditory systems. The AIADH seems to detect auditory symptoms associated with solvent exposure even before they can be detected by pure-tone audiometry. In the study conducted by Fuente et al[29] all participants (exposed and unexposed) presented with normal audiometric hearing thresholds and yet solvent-exposed workers showed significantly worse AIADH scores than those not exposed to solvents. Fuente et al[29] suggested that the AIADH should be used in hearing conservation programs to screen for possible negative auditory outcomes due to solvent exposure that are not detected by pure-tone audiometry. The AIADH was initially developed in Dutch and English[48] and later adapted into Spanish,[50] Cantonese,[51] Portuguese,[52] and Turkish.[53]

## Pure-Tone Audiometry

Pure-tone audiometry was the most frequently used audiological test investigating the effects of solvents on the human auditory system (25 of 37 studies). Several studies demonstrated abnormalities in other auditory tests of workers exposed to

**Table 3 Statistical differences between solvent-exposed and nonexposed workers of audiological outcomes for 13 epidemiological studies: results for electroacoustic tests**

| Study | ART | | | ARD | | | SOE | | | TEOAE | | | SETEOAE | | | DPOAE | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | NSD | SIG | NR | NSD | SIG | NR | NSD | SIG | NR | NSD | SIG | NR | NSD | SIG | NR | NSD | SIG | NR |
| Morata et al[59] | | x | | | x | | | | | | | | | | | | | |
| Calabrese et al[34] | x | | | | | | | | | | | | | | | | | |
| Morata et al[61] | x | | | | x | | | | | | | | | | | | | |
| Sułkowski et al[63] | | | x | | | | | | x | | x | | | | | | x | |
| Prasher et al[62] | x | | | | | | | | | | | x | | | | | | x |
| Fuente et al[37] | | | | x | | | | | | | | | | | | | | |
| Johnson et al[68] | | | | | | | | | | | | | | | | x | | |
| Quevedo et al[39] | | | | | | | | | | x | | | | x | | | | |
| Fuente et al[69] | | | | | | | | | | | | | | | | x | | |
| Fuente et al[16] | | | | | | | | | | | x | | | | | | | |
| Chiaramello et al[31] | | | | | | | | | | | x | | | | | | | |
| Roggia et al[60] | | x | | | | | | | | | x | | | | | | x | |
| Sliwinska-Kowalska et al[56] | | | | | | | | | | | | | | | | | x | |
| Total | 3/6 | 2/6 | 1/6 | 1/3 | 2/3 | 0/3 | 0/1 | 0/1 | 1/1 | 1/6 | 4/6 | 1/6 | 0/1 | 1/1 | 0/1 | 2/6 | 3/6 | 1/6 |

Abbreviations: NSD, no statistical difference; SIG, statistically significant difference; NR, not reported (included all studies where the authors did not report test results, or if they did not mention whether there was a statistical difference between the groups); ART, acoustic reflex thresholds; ARD, acoustic reflex decay; SOE, spontaneous otoacoustic emissions; TEOAE, transient-evoked otoacoustic emission; SETEOAE, suppressive effect of TEOAE; DPOAE, distortion product otoacoustic emissions.

solvents even in subjects presented with normal audiometric hearing thresholds.[20,34,37,39,54] In addition to the 25 included studies which used it, 14 studies were excluded because they only used that test. It should be noted that 12 of the excluded studies detected an effect of solvents by comparing rates of hearing loss across different exposure groups. Several authors have argued that pure-tone audiometry is not sufficient for a complete evaluation of the auditory performance of workers exposed to solvents, and not likely to detect early auditory signs of solvent exposure.[1,16,18,28]

Several studies have found significantly poorer audiometric hearing thresholds in solvent-exposed workers than unexposed participants, even when they were classified as normal-hearing thresholds.[16,20,28,29] Thus, pure-tone audiometric results can still contribute to the decision for a referral. If a worker exhibits hearing thresholds within the normal range (0–25 dB) but the individual complaints of listening difficulties that cannot be explained by the audiogram, then this worker should be referred for a comprehensive audiological assessment.

Only three studies used extended high-frequency audiometric testing to investigate the effects of solvent exposure on the human auditory system.[30,55,56] The limited utilization of this audiometric methodology was unexpected since extended high-frequency pure-tone audiometry is one of the recommended procedures for ototoxicity monitoring.[57,58] Among the three included studies, only one of them showed significantly worse results in workers exposed to solvents than in unexposed participants.[56] The large intersubject variability inherent to ultra-high-frequency hearing thresholds[58] could explain the absence of significant differences in two of the three studies that used this auditory test. Future studies with the aim to determine possible associations between solvent exposure and changes in high or ultra-high-frequency thresholds should prioritize longitudinal study designs.

## Speech Audiometry

The Word Recognition in Quiet was the only speech audiometric test cited by 3 of the 37 studies.[32,33,35] None of these studies found a significant difference between solvent-exposed and unexposed participants. These results suggest that speech recognition in quiet is likely to be unaffected by solvent exposure and therefore this procedure does not add to an audiological test battery to be used with solvent-exposed workers. See the behavioral tests used to assess auditory processing skills

**Table 4 Statistical differences between solvent-exposed and nonexposed workers of audiological outcomes for 23 epidemiological studies: results for electrophysiological tests**

| Study | ABR | | | CRA | | | LAEP | | | P300 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | NSD | SIG | NR | NSD | SIG | NR | NSD | SIG | NR | NSD | SIG | NR |
| Antti-Poika et al[75] | x | | | | | | | | | | | |
| Möller et al[32] | | | | | | x | | | | | | |
| Massioui et al. (1990)[73] | | x | | | | | x | | | x | | |
| Möller et al[33] | | | | | | x | | | | | | |
| Morrow et al. (1992)[44] | | | | | | | | x | | | x | |
| Abbate et al. (1993)[54] | | x | | | | | | | | | | |
| Deschamps et al[40] | x | | | | | | | | | | | |
| Lille et al[41] | x | | | | | | | | | | | |
| Araki et al[42] | x | | | | | | | | | x | | |
| Calabrese et al[34] | x | | | | | | | | | | | |
| Vrca et al[74] | | x | | | | | | | | | | |
| Kumar and Tandon[43] | x | | | | | | | | | | | |
| Steinhauer et al[45] | | | | | | | x | | | | x | |
| Niklasson et al[35] | | | | | x | | | | | | | |
| Moshe et al[36] | | x | | | | | | | | | | |
| Prasher et al[62] | x | | | | | | | | | | | |
| Johnson et al[68] | | | | | x | | | | | | | |
| Keski-Säntti et al[46] | | | | | | | | | | | x | |
| Keski-Säntti et al[47] | | | | | | | | | | | x | |
| Fuente et al[69] | | x | | | | | | | | | | |
| Juárez-Pérez et al[55] | | x | | | | | | | | | | |
| Roggia et al[60] | | x | | | | | | | | x | | |
| Sliwinska-Kowalska et al[56] | | x | | | | | | | | | | |
| Total | 7/15 | 8/15 | 0/15 | 0/5 | 2/5 | 3/5 | 2/3 | 1/3 | 0/3 | 3/7 | 4/7 | 0/7 |

Abbreviations: NSD, no statistical difference; SIG, statistically significant difference; NR, not reported (included all studies where the authors did not report test results, or if they did not mention whether there was a statistical difference between the groups). ABR, auditory brainstem responses; CRA, cortical response audiometry (includes all studies in which authors described the test as CRA and evoked-related potential were not specified); LAEP, late auditory evoked potentials (includes studies with one or more of the following components: N1, N100, N2, N200, N250, P1, P2); P300, includes P3.

session for information on other tests that used speech stimuli.

### Acoustic Reflex Thresholds and Acoustic Reflex Decay

ARTs were investigated in six studies. Two studies found significant differences between workers exposed and unexposed to solvents[59,60] but three studies did not.[34,61,62] One study did not report its results.[63] Roggia et al[60] found that workers exposed to gasoline had significantly worse ARTs and a greater number of absent reflexes than nonexposed participants. Considering that ARTs are typically elevated or absent with the stimulus to the affected ear in cases of retrocochlear pathologies, or eighth cranial nerve lesions,[64] the abnormal results could indicate an effect of the solvent exposures.

Elevated or absent ART were found in workers with hearing thresholds within the normal range in audiometry, but with a history of exposure to gasoline,[60,65,66] which suggests that this test may be more sensitive than pure-tone audiometry for detecting the effects of solvents on the auditory system. The ART is common in clinical audiology practice, as it is a simple, quick procedure that does not depend on sophisticated equipment. However, it is necessary to keep in mind that ART measurements are often not reliable because of limitations of the equipment (few parameters are user modifiable, and the impedance probes are often not sensitive enough). The result is that many unexposed,

**Table 5 Statistical differences between the results from behavioral test used to assess auditory processing skills from solvent-exposed and nonexposed workers of audiological outcomes for 13 epidemiological studies**

| Study | DD | | | FS | | | HINT | | | IS | | | MLD | | | PPS | | | RGD | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | NSD | SIG | NR | NSD | SIG | NR | NSD | SIG | NR | NSD | SIG | NR | NSD | SIG | NR | NSD | SIG | NR | NSD | SIG | NR |
| Möller et al[32] | | | | | | | | | | | | x | | | | | | | | | |
| Möller et al[33] | | | | | | | | | | | | x | | | | | | | | | |
| Niklasson et al[35] | | | | | | | | | | | x | | | | | | | | | | |
| Fuente et al[37] | | x | | | x | | | x | | | | | x | | | | x | | | x | |
| Johnson et al[68] | | | | | | | | | | x | | | | | | | | | | | |
| Fuente and McPherson[38] | | | | | x | | | x | | | | | | | | | | | | x | |
| Fuente and McPherson[28] | | x | | | x | | | x | | | | | | | | | x | | | x | |
| Zamyslowska-Szmytke et al[80] | | | | | | | | | | | | | | | | | x | | | | |
| Fuente et al[20] | | x | | | x | | | x | | | | | x | | | | x | | | x | |
| Fuente et al[69] | | x | | | | | | x | | | | | x | | | | x | | | | |
| Fuente et al[16] | | | | | | | | x | | | | | | | | | | | | x | |
| Fuente et al[29] | | | | | | | | | | | | | | | | | | | | x | |
| Landry and Fuente[8] | | x | | | | | | | | | | | | | | | | | | | |
| Total | 0/5 | 5/5 | 0/5 | 0/4 | 4/4 | 0/4 | 0/6 | 6/6 | 0/6 | 1/4 | 1/4 | 2/4 | 3/3 | 0/3 | 0/3 | 0/5 | 5/5 | 0/5 | 0/6 | 6/6 | 0/6 |

Abbreviations: NSD, no statistical difference; SIG, statistically significant difference; NR, not reported (included all studies where the authors did not report test results, or if they did not mention whether there was a statistical difference between the groups); DD, dichotic digit; FS, filtered speech; HINT, Hearing In Noise Test; IS, interrupted speech; MLD, masking level difference; PPS, Pitch pattern sequence; RGD, Random Gap Detection.
Notes: Five other tests not shown in Table 5 were used only in one study. Two tests, the Psycho-acoustical modulation transfer function (PMTF) and Speech recognition in noise (SRN) tests, were used in one study (Johnson et al, 2006);[68] both showed statistically significant differences between the groups. The Duration Pattern (DP) and Gaps In Noise (GIN) tests were used in one study (Zamyslowska-Szmytke et al, 2009);[80] the DP showed statistically significant differences between the groups; however, the GIN did not show statistical differences. The ATTR (Adaptive Tests of Temporal Resolution) test was used in only one study (Fuente et al, 2013);[69] it did not show statistical differences between the groups.

normal hearing subjects may display very high reflex thresholds. Epidemiological and clinical studies are needed on its use in the early detection of the effects of solvents on the auditory system.

Only three studies measured the acoustic reflex decay. Two of these studies found significant differences between participants exposed and unexposed to solvents,[59,61] while one study[37] did not. While acoustic reflex decay results could indicate retrocochlear or central auditory dysfunction among subjects exposed to chemicals, its use has been questioned today due to the high intensity of the stimulus that are necessary in the test.[67]

## Otoacoustic Emissions

TEOAEs were used in six studies and DPOAEs in other six studies. TEOAE amplitudes were lower (i.e., poorer) among solvent-exposed workers than unexposed participants in four studies,[16,31,60,63] one did not find significant differences between groups,[39] and one of them did not report if differences were found.[62] Regarding DPOAE, three studies reported lower DPOAE amplitudes for the samples of workers exposed to solvents than the control groups.[56,60,63] Two studies did not find significant differences between groups for this auditory outcome,[68,69] and one study did not report the statistical test results.[62]

In summary, most of the studies have found an effect of solvent exposure on otoacoustic emissions (OAEs). These results are consistent with animal studies which have consistently found that solvents adversely affect the outer hair cell in the cochlea.[70] OAEs have also been shown to be useful in the early detection of cochlear dysfunctions induced by solvents,[16,60,71] as well as in monitoring the cochlear functioning of workers exposed to solvents,[56] and may be considered a biomarker of inner ear dysfunction associated with exposure to organic solvents.[71]

Thus, consideration should be given to incorporating OAE testing in the audiological test battery to evaluate workers exposed to solvents, as they provide information on the functional integrity of the outer hair cells[72] which are likely to be affected by solvent exposure. Dhar and Hall[72] when reviewing the contributions of OAEs suggested that this procedure can detect early signs of cochlear dysfunction. Future longitudinal studies should be carried out with the aim to determine possible associations between solvent exposure levels and changes in OAEs. Such studies may provide guidelines on how to use OAEs to identify red flags that will prompt further actions. The use of OAEs in the context of hearing conservation programs would require diagnostic equipment, trained personnel, and extra time in testing workers, which are some of the barriers for its implementation in the occupational setting.

## Auditory Evoked Potentials

The ABR was used in 15 out of the 37 articles included in this review. Eight studies reported significant differences between exposed and unexposed participants,[36,54–56,60,69,73,74] while seven studies did not.[34,40–43,62,75] Six studies presented results suggestive of auditory pathway impairment in the brainstem,[36,55,60,62,69,73] two studies have demonstrated alterations suggestive of both peripheral and central auditory impairment,[54,74] and one study showed peripheral impairment.[56] It is also important to highlight that in six studies, the results were suggestive of central auditory impairment even though the subjects presented all audiometric thresholds within normal limits, or only mild hearing loss in some frequencies.[36,54,55,60,62,69]

The majority of the included studies which used ABRs only analyzed the most common parameters used in the clinic for the interpretation of the results, that is, the absolute latencies of waves I, III, and V and the I–III, III–V, and I–V interpeak latencies. ABR amplitudes have been investigated only in four studies,[40,60,73,74] but three of them[60,73,74] reported significantly smaller ABR waves among solvent-exposed participants than in nonexposed, suggesting a predominantly central auditory dysfunction[60,73,74] or peripheral dysfunction.[74] The analysis of the ABR amplitude seems to be a sensitive parameter to detect abnormalities. Considering that few human studies have analyzed this ABR parameter, it is suggested that it should be included in future studies with workers exposed to solvents.

The ABR provides information on the functioning of the auditory nerve and the auditory pathway in the brainstem,[76] allows the identification of both peripheral and central auditory dysfunctions,[77] and is considered the most clinically useful auditory evoked potential.[78] The evidence from the included studies which used ABR suggests therefore that this audiological test can be useful for the early detection of the effects of the solvents on the human auditory system. In addition, ABR could also help differentiate the effects of noise from the effects of chemicals, considering that ABR results have not often been reported to be associated with occupational noise exposure.[79] Studies with more detailed exposure information are necessary since ABR did not show significant differences between participants in seven of the fifteen studies included in this review.[34,40–43,62,75]

Electrophysiological measures other than the ABR have also been used to investigate the effects of solvent exposure on the human central auditory system. All of them were cortical evoked potentials. We used the terminology "cortical response audiometry (CRA)" to all studies where the authors named the test as CRA and when the evoked-related potential (ERP) components were not specified in the articles. We used the terminology "late auditory evoked potentials (LAEP)" to all studies that analyzed one or more of the following ERP components: N1, N100, N2, N200, N250, P1, and P2. We also identified the studies where P300 was measured.

P300 was used in seven studies,[42,44–47,60,73] CRA in 4 studies,[32,33,35,68] and LAEP in three studies.[44,45,73] The P300 is a positive peak that occurs at around 300 milliseconds after stimulus presentation when an oddball paradigm is used. Four studies found significant differences between exposed and nonexposed participants for the P300.[44–47] In two studies, participants exposed to solvents showed longer P300 latencies than nonexposed participants[44,45]; in one study, the P300 amplitude was smaller[47]; and in one study, the P300 amplitude was smaller and its latency was longer.[46] No significant differences between groups were found for P300 in three studies.[42,60,73]

Significant differences were found between participants exposed and nonexposed to solvents in only two studies that mentioned having used CRA,[35,68] and only in one study that recorded LAEP.[44] Participants exposed to solvents showed longer CRA latencies than nonexposed participants in two studies,[35,68] as well as increased N100 and P200 amplitudes, and longer N250 latency in one study.[44]

### Behavioral Tests Used to Assess Auditory Processing Skills

Overall, 12 different behavioral procedures to evaluate the CANS were used in the included studies. Three were tests of temporal resolution: ATTR[69]; RGD test[16,20,28,29,37,38]; Gaps-in-Noise (GIN) test[80]; DD test[8,20,28,37,69]; two tests to evaluate temporal processing, specifically temporal patterning and ordering—DPS test[80] and PPS test[16,20,28,29,37]; one test to evaluate binaural interaction—MLD[20,37,69]; two tests to evaluate the auditory closure—FS test[20,28,37,38] and Interrupted Speech (IS) test[32,33,35,68]; and three tests to evaluate sound segregation and auditory closure—HINT,[16,20,28,37,38,69] PMTF,[68] and the Swedish Speech Recognition in Noise.[68] The most used tests to evaluate the CANS were the HINT and RGD, used in six studies. Then, the DD and PPS tests were used in five studies, and the FS test was used in four studies. Most of the studies found significant differences between groups for the tests used to evaluate the CANS. The tests that consistently showed differences between groups were the HINT, the RGD, the DD, the PPS, and the FS which showed significantly poorer results in participants exposed to solvents than in nonexposed in all studies in which they were used. The IS test showed significant differences between solvent-exposed and nonexposed participants in only one study,[35] and the MLD test did not find significant differences between solvent-exposed and nonexposed participants in any of the three studies in which it was used.[20,37,69] In summary, most studies[8,16,20,28,29,37,38] have shown significantly poorer auditory processing skills in workers exposed to solvents than in nonexposed even in the presence of audiometric thresholds considered to be within normality classifications.

The analysis of the results obtained in the behavioral tests used for the assessment of auditory processing suggests, therefore, that solvents can affect the vast majority of auditory processing skills, given that the only test that did not show poorer auditory processing skills in participants exposed to solvents than in nonexposed was the MLD (a test that evaluates the ability of binaural interaction). It should be noted, however, that the MLD test was used in only three studies.[20,37,69]

The results obtained in this review suggest that the most effective tests for detecting the effects of solvents on the auditory system are the HINT and the RGD, followed by the DD and the PPS. However, considering the number of tests that evaluate behavioral assessment of auditory processing, as well as the small number of studies that each of the existing tests was applied to workers exposed to solvents, more research would help determine which of these would be most useful for the early detection of the effects of solvents on the auditory system. Furthermore, the choice of test(s) to be used must also consider the feasibility of application in the specific clinical context.

## QUALITY AND IMPLICATIONS OF THE EVIDENCE

This mixed review method used techniques from both scoping reviews and systematic reviews and described the volume of literature available as well as an overview of the focus of included studies. The quality assessment for included studies identified how far primary research evidence, singly and collectively, could inform clinical practice recommendations for audiologists who encounter patients with hearing complaints which may be due to occupational or other chemical ototoxicity. The evaluation for the quality of each of these 37 individual studies was considered low to moderate. The overall quality of the evidence together was considered low due to their study designs (either cross-sectional studies or case–control).

In addition to being limited by the quality of research reported, this review had another limitation worth acknowledging. Publication bias may be influencing the results synthesized here and the degree to which these impacts would be seen is difficult to assess or quantify. However, given the greater likelihood of studies with statistically significant findings to face fewer obstacles during the publication process, we might expect studies with positive outcomes to be overrepresented to some degree and studies with negative or inconclusive results to be underrepresented.

We included *p*-values when reported by the authors of studies as a method to compare results across these different study designs inclusively. However, it should be noted that *p*-values can be arbitrary and studies showing results which are not significant statistically should not always be dismissed as they may conceal potentially important public health effects.[24] Effect sizes (such as risk ratios and corresponding confidence intervals) were rarely reported in these 37 studies. Future research investigating solvent ototoxicity should be encouraged to calculate effect sizes and report these values as they improve power calculations, estimations for target sample sizes, and facilitate clinical interpretations as well as decision-making in risk assessments. However, effect sizes are scale dependent; so, comparisons across different scales or outcome measures are more challenging.

Many barriers hinder the implementation of using a variety of audiological tests in occupational settings, but we hope that newer technologies and this review can help narrow down to a few test alternatives. In particular, we recommend occupational health practitioners use self-report listening questionnaires, especially in combination with pure-tone audiometric results. A self-report of an individual's listening performance in a variety of settings and to different types of sounds offers additional information to guide judgments on the need for further audiological testing and referrals. This review demonstrates the importance of routinely gathering noise and chemical exposure information, both occupational and recreational, from patients by hearing health professionals in clinical settings; this review also has summarized selection of testing options to use for solvent-exposed patients. For additional information on possible actions in the occupational setting, see Morata et al (2022).[81]

The absence of strong conclusive evidence means further research in the field of occupational ototoxicity assessment will have an important impact. Limitations in providing conclusions generalizable to other populations from these studies include the differences in chemical (and noise) exposures; the paucity of information described regarding current and past exposures histories (to both solvents and noise); and the variety of audiological testing methodologies performed.

Due to the state of the literature it is unfeasible to conduct a full systematic review and meta-analysis at this point in time. However, there is a growing consensus that evidence-based practices should involve the integration of the highest quality and most current research findings with clinical/educational expertise and relevant stakeholder perspectives.[22,23] The evidence synthesized in this review might facilitate the decision making of which clinical tools to use in the diagnoses of ototoxicity and central auditory dysfunctions associated with solvent exposures.

## CONCLUSION

The 37 articles reviewed here demonstrate that a variety of tests have been used to evaluate many aspects of auditory function in workers exposed to solvents. The majority of evidence from these studies utilized pure-tone audiometry and/or ABR to evaluate the auditory system in solvent-exposed workers. Not all these tests are likely to be available in all clinical settings. Few studies used the AIADH self-report questionnaire, or assessed auditory processing skills through the DD, FS, HINT, PPS, or RGD behavioral tests. All studies which used these six tests reported significant differences among solvent-exposed groups, so we suggest future research and clinical practice focus on these tests. Gaps in this body of literature include a lack of high-quality studies using a randomized design or a longitudinal design. These types of studies would obtain more detailed information on current exposure indicators as well as occupational exposure histories and thereby establish a greater rigor in selecting comparison subgroups. Current evidence, however, allows us to identify the type of auditory dysfunctions to be expected and characteristics that an audiological test battery for solvent-exposed workers should have. Furthermore, information provided by the current review should facilitate the development of high-quality studies in the future to better address these existing gaps and limitations. Finally, the absence of conclusive evidence should not be interpreted as evidence of lack of effectiveness for the audiological methodologies studied. Rather, it means that further research in occupational ototoxicity determination is very likely to have an important impact.

## CONFLICT OF INTEREST

None declared.


## ACKNOWLEDGEMENTS AND DISCLAIMER

Dr. David Byrne from the National Institute for Occupational Safety and Health (NIOSH) and Dr. Robert Keith from the University of Cincinnati provided helpful critiques of the manuscript. The topic of this article became part of an initiative of the International Ototoxicity Monitoring Group (IOMG): "To conduct an environmental scan of test measures currently used to identify ototoxicity from environmental and occupational exposures." This work was led by IOMG Chair, T.C.M., and conducted by other working group members as well as scientists and students who are not formally affiliated with IOMG. The study was supported in part by a grant from CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico of the Ministry of Science, Technology and Innovation of Brazil) for S.M.R. The findings and conclusions in this report are those of the author (s) and do not necessarily represent the official position of the NIOSH, Centers for Disease Control and Prevention (CDC). Mention of any company or product does not constitute endorsement by the NIOSH, CDC.


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**Appendix Table A1 Description of study designs, auditory testing results, and system affected/conclusions for 37 epidemiological studies on solvent ototoxicity**

| Reference | Study design/Population/Exposure | Auditory tests/results | System affected/Conclusions |
|---|---|---|---|
| Muijser et al[30] | Cross-sectional study<br>- 59 workers; styrene; exposed to noise levels below 85 dB (regularly) and above 85 dB (occasionally for short periods).<br>- 88 control subjects exposed to noise ranged from 80 to 85 dB | PTA: There was no significant difference between groups.<br>HFA/There was no significant difference between groups, but there was statistically significant difference in high-frequency thresholds within the experimental group (less exposed and more exposed workers) | PAS (results suggest that styrene exposure may affect hearing thresholds at high frequencies) |
| Antti-Poika et al[75] | Cross-sectional study<br>- 48 workers; toluene, xylene, petroleum benzine, ethanol, butanol, ethyl and butyl acetate, methyl isobutyl ketone, and dichloromethane.<br>- 40 control subjects | PTA: 60% exposed and 42% controls had normal audiograms<br>ABR: ABR findings classified as abnormal were more common in the exposed group than among the referents and in the persons who used alcohol than in the non-users. There were no statistically significant differences in the absolute values of ABR interpeak latencies between the exposed and unexposed | Inconclusive results (due to the small number of subjects examined, the study was inconclusive); the differences were not statistically significant, and no exposure–response relationships were found |
| Möller et al[32] | Case–control study<br>- 9 subjects with long-term occupational exposure to industrial solvents and a confirmed diagnosis of psycho-organic syndrome; mixtures of alcohol, aromatic and aliphatic industrial solvents.<br>- 9 control subjects | PTA and maximum speech discrimination: They did not indicate hearing losses.<br>Discrimination of interrupted speech and CRA delta-f/ abnormal results in 44% in psycho-organic syndrome group | CANS (the test battery used strongly indicates central nervous system lesions due to industrial solvents) |
| Massioui et al[73] | Case–control study<br>- 13 workers who suffered from an organic psychosyndrome, toluene, xylene, gasolines, naphthas, kerosines, trichloroethane, trichloroethylene, methylene chloride.<br>- 26 patients from an alcoholic group.<br>- 20 control subjects | ABR: Solvent exposure—there was no effect on ABR latencies; significant decrease of wave V amplitude in both study groups.<br>Cognitive ERP components (N1, N2, and P3): There was no significant difference between groups for morphology, latency, and amplitude; reaction times of workers exposed to solvent were significantly increased compared to controls and alcoholics; solvent and alcoholic groups made significantly more errors (either false alarms or misses) than controls | PAS and CANS (the results support the presence, in solvent-exposed workers, of a minor dysfunction of the nervous system at both peripheral and cortical levels potentiated by alcohol as well as of mild cognitive impairments concerning attention processes) |

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| Reference | Study design/Population/Exposure | Auditory tests/results | System affected/Conclusions |
|---|---|---|---|
| Möller et al[33] | Cross-sectional study<br>- 18 workers; styrene<br>- 18 control subjects.<br>- 52 workers from the construction industry, unexposed to industrial solvents | PTA, speech discrimination (maximum speech discrimination of 50 monosyllabic words; discrimination of interrupted speech with three interruption rates (4, 7, and 10/s) and CRA/PTA and speech discrimination scores did not indicate hearing losses due to causes other than age and/or exposure to noise. Seven workers displayed abnormal results in distorted speech and/or the CRA | CANS (styrene exposure at moderate or low levels causes central nervous system disturbances which are not always diagnosable with psychometric tests) |
| Morrow et al[44] | Case–control study<br>- 12 workers with toxic encephalopathy; toluene and trichloroethylene.<br>- 19 control subjects | N100, P200, and N250: N100–P200 difference at Cz: significantly larger response in the solvent-exposed group; the N250 mean latency increased for the solvent-exposed group.<br>P300/solvent group: latency showed a longer duration; significantly delay P300 latencies as compared with controls | CANS (the assessment of event-related potentials may be an especially useful way to evaluate CANS integrity in persons who have had a neurotoxic exposure) |
| Abbate et al[54] | Cross-sectional study<br>- 40 workers exposed to toluene.<br>- 40 control subjects.<br>- Only participants with normal hearing thresholds were included in both groups | ABR: The mean latencies of all waves and interpeak were statistically significantly higher in the exposed group; toluene exposure: effect on all the waves, but wave I showed the biggest correlation effects with both rate of presentations used | PAS and CANS (ABR can demonstrate auditory nervous system modifications even before the occurrence of clinical signs due to chronic exposure to toluene; no hearing problems were observed, but only ABR was done) |
| Deschamps et al[40] | Case–control study<br>- 50 workers; organic solvents.<br>- 40 control subjects | ABR: The parameters studied (interpeak latency and ratios of amplitudes of waves I/V) did not differ significantly between the groups | No hearing problems were observed, but only ABR was done |
| Lille et al[41] | Cross-sectional study<br>- 46 workers; toluene, xylene, gasolines, naphthas, kerosines, trichloroethane, trichloroethylene, methylene chloride.<br>- 40 control subjects | ABR: No differences were found between groups | No hearing problems were observed, but only ABR was done; results confirm the absence of the sensitivity of ABR to solvent exposure |

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| Reference | Study design/Population/Exposure | Auditory tests/results | System affected/Conclusions |
|---|---|---|---|
| Morata et al[59] | Cross-sectional study<br>- 50 workers not exposed to noise.<br>- 50 workers exposed to noise.<br>- 51 workers exposed to noise and toluene.<br>- 39 workers exposed to organic solvent mixture | PTA: The risk of hearing loss was greater for the exposed groups; the adjusted relative risk estimates were four times greater for the noise group, two times greater for the noise and toluene group, and five times greater for the solvent-mixture group.<br>Immittance audiometry: There were significant differences between the groups regarding recruitment and reflex decay, but not absence or elevation of reflex | PAS and CANS (the audiological results of the noise and toluene group suggest a central auditory pathway involvement in the hearing losses observed) |
| Araki et al[42] | Cross-sectional study<br>- 22 workers exposed to lead (gun metal foundry)<br>- 13 workers (rotogravure printing company)<br>- 51 workers (exposed to local vibration).<br>- 11 workers (toluene, methyl ethyl ketone, methanol, xylene, and n-hexane)<br>- 12 workers (styrene).<br>- 24 female key punchers and 6 female university students | ABR: Delay in ABR latency (I–V and V) in vibrating tool workers as well as significant correlations of BAEP latency with length of work in group exposed to local vibration (brush saw operators);<br>P300: The latency in all gun metal foundry workers was prolonged and significantly correlated with blood lead concentrations and urinary lead concentrations in the workers | CANS (prolonged latencies in the P300 test were observed only among workers exposed to lead) |
| Calabrese et al[34] | Cross-sectional study<br>- 20 workers exposed to styrene and acetone.<br>- 10 control subjects | PTA: All workers examined had a normal hearing threshold.<br>ART: No abnormalities of acoustic reflex were found.<br>ABR: The mean values of the groups were not significantly different for any of the variables (wave and interpeak latencies); after the recovery period, considerable changes in ABRs were not found | No permanent significant effect in any of the hearing tests |
| Vrca et al[74] | Cross-sectional study<br>- 49 workers; toluene.<br>- 59 control subjects | ABR: The latency of all waves was significantly longer, and the amplitude was significantly smaller in exposed subjects; significant differences were found between the groups in III–IV, I–IV, I–V, and III–V interpeak latencies | PAS and CANS (ABR could be included in pre-employment examinations for workplaces where toluene exposure is anticipated and biological effects monitored by follow-up examinations, depending on the concentration of the toxic agent) |

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| Reference | Study design/Population/Exposure | Auditory tests/results | System affected/Conclusions |
|---|---|---|---|
| Kumar and Tandon[43] | Cross-sectional study<br>- 40 rubber factory workers.<br>- 20 control subjects | ABR: No significant differences in any parameter between the groups; however, the 40 workers (80 ears) tested had abnormalities in ABR, i.e., in either of prolongation of peak latencies beyond mean +2 SD of normal or IPL beyond mean +3 SD of normal | CANS (results suggested that the rubber factory environment does affect the auditory pathway in the brainstem) |
| Morata et al[61] | Cross-sectional study<br>- 438 petroleum refinery workers exposed to benzene, toluene, xylene, ethyl benzene, and cyclohexane; noise levels were less than 85 dB TWA, except in the aromatics, paraffins and maintenance groups.<br>- 41 control subjects | PTA: The prevalence of hearing loss in the exposed groups was significantly higher than in the control groups (42–50%); high-frequency hearing loss: more significantly in the exposed groups when compared with control or laboratory groups.<br>ART: No significant differences between the groups regarding absence or elevation of the reflex.<br>Reflex decay test: Significant differences between the groups | PAS and CANS (ART strongly suggested that the site and the mechanisms underlying the lesions from noise + chemical are different from noise exposure alone; acoustic reflex decay test suggests retrocochlear or central auditory pathway in subjects exposed to chemicals; these battery tests can be useful screening tools to investigate hearing disorders in complex exposure) |
| Steinhauer et al[45] | Cross-sectional study<br>- 35 Journeymen painters.<br>- 41 controls subjects | Auditory ERPs (P300, N100, P200, and N250): P300 latency to target stimuli was significantly longer for acute painters; P300 amplitude did not differ significantly among groups or between tasks; no group effects were associated with N100 or P200 amplitude | CANS (P300 latency may be an optimal indicator for the effectiveness of protective equipment for blocking the deleterious effects of hazardous chemicals on brain function) |
| Niklasson et al[35] | Case–control study<br>- 60 workers with suspicion of solvent-induced chronic toxic encephalopathy; white spirits, thinner, toluene, and xylene.<br>- 18 control subjects | PTA: There was no difference between the groups regarding the relative number of hearing threshold levels falling outside the 5 or 10 percentiles for age-related hearing thresholds.<br>Speech recognition of monosyllabic words: Normal results in all groups. | CANS (the audiological test profile demonstrated a cortical impairment of the hearing pathways likely in subjects in solvent-exposed workers) |

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| Reference | Study design/Population/Exposure | Auditory tests/results | System affected/Conclusions |
|---|---|---|---|
| | | Speech recognition for distorted speech (interrupted speech): The scores were significantly lower in the solvent group.<br>CRA: The latencies were significantly longer in the solvent group | |
| Moshe et al[36] | Cross-sectional study<br>- 40 workers exposed to mercury.<br>- 37 workers exposed to chlorinated hydrocarbons.<br>- 36 control subjects | PTA: There was no statistically significant difference between the two groups for all tested frequencies. The hearing thresholds for both studied groups at 0.25–2 kHz ranged from 15 to 19 dB.<br>- The mean threshold at 4 kHz and at 6 kHz in both ears was, respectively:<br>- Mercury group: 25 and 23.2 dB HL;<br>- Chlorinated hydrocarbons group: 28.8 and 30.3 dB HL;<br>- Controls: 24 and 23.3 dB HL.<br>ABR: A significant difference was found in the IPL I–III in the study groups compared to the control group. The proportion of abnormal findings in IPL I–III was 42.5% in the mercury workers, 33.8% in the CH workers, and 18.0% in the control group | PAS and CANS (ABR may provide a sensitive tool for detecting subclinical central neurotoxicity caused by chlorinated hydrocarbons and mercury) |
| Sułkowski et al[63] | Cross-sectional study<br>- 61 workers exposed to xylene, toluene, ethyltoluene, styrene, n-propylbenzene, and (mostly) trimethylbenzene isomers: pseudocumene, mesitylene and hemimetillene.<br>- 40 control subjects | PTA: Hearing thresholds closely corresponded with cumulative dose of exposure (with the increased dose, highest thresholds were observed).<br>ART: The results were not presented.<br>TEOAE and DPOAE: Amplitudes significantly reduced in the study group, corresponding to the cumulative dose of exposure (higher exposure, lower amplitude of EOEs)<br>SOAE: Low percentage of SOAE present in both studied groups | PAS (The results provide convincing evidence that occupational exposure to a mixture of organic solvents is ototoxic—the observed symptoms of the inner ear damage in the subjects under study can be attributed to the long-term exposure to mixtures of solvents) |

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| Reference | Study design/Population/Exposure | Auditory tests/results | System affected/Conclusions |
|---|---|---|---|
| Prasher et al[62] | Cross-sectional study<br>- 174 aircraft maintenance workers exposed to benzene, n-hexane, toluene, xylenes, naphthalene, trichloroethane, dimethylacetamide, and noise.<br>- 153 exposed only to noise.<br>- 13 exposed only to solvents.<br>- 39 control subjects | PTA: Control and solvents group—similar mean age and mean thresholds, but 33.3% of the solvent group had a hearing loss compared to 5.6% of the controls. The noise-alone group had a greater mean loss of 35.3 dB compared to solvents + noise group of 20.8 dB; there was a significant effect on pure-tone thresholds for both noise and solvents + noise.<br>ART: The mean acoustic reflex thresholds showed a pattern of differences which differentiate noise from solvent and noise groups; the contralateral pathway appears to be differentially affected by solvent exposure.<br>DPOAE: It declined with frequency and exhibited lower amplitude with noise compared to solvents + noise group; both groups showed recovery from 6 kHz upward, with reversal more prominent for the noise group, reflecting a highly significant interaction.<br>TEOAE: Reproducibility—the main effect of frequency was highly significant, as was the main effect of the exposure group; TEOAE S/N ratio—the noise group was more affected; the highly significant main effect of frequency reflected the peak at 1.5 kHz.<br>ABR: 32.4% of subjects had abnormally prolonged inter-wave interval (I–V) in the solvent and noise group. There was no difference in the mean latencies for all waves for the groups | PAS and CANS (the effect of a mixture of solvents on the auditory system appears to occur both at the end organ level as well as in the nervous pathway) |
| Fuente et al[37] | Cross-sectional study<br>- 10 workers; toluene, xylene, and n-hexane; noise level was lower than 85 dBA.<br>- 10 control subjects | PTA: Normal hearing thresholds at the frequencies tested; no statistically significant differences between groups.<br>Acoustic reflex decay: None of the subjects presented abnormal results.<br>DD, FS, and PPS: Workers exposed to solvents obtained significantly lower scores than nonexposed. | CANS (despite having normal hearing thresholds and speech recognition thresholds, results for central auditory tests were abnormal in a group of workers exposed to solvents) |

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| Reference | Study design/Population/Exposure | Auditory tests/results | System affected/Conclusions |
| --- | --- | --- | --- |
| | | MLD: No statistically significant difference in test scores between the groups.<br>RGD: Control group—significantly lower (better) gap detection thresholds than the exposed group in 500 Hz, 1,000 Hz, and 2,000 Hz.<br>HINT: Control group showed significantly better SNRs in comparison with the exposed group for HINT 1 and for HINT composite score | |
| Johnson et al[68] | Cross-sectional study<br>- 65 workers exposed to noise.<br>- 89 to styrene only.<br>- 81 to styrene and noise.<br>- 78 control subjects | PTA: Significantly higher thresholds at 2, 3, 4, and 6 kHz in the styrene group in both ears, compared with the other groups.<br>PMTF: Statistically significant differences existed between noise (alone or with styrene) and non-noise exposed (with or without styrene) groups.<br>DPOAE: Signal levels up to 50 dB—control and noise groups had higher DPOAE levels compared to the other groups; signal levels past 50 dB—controls showed lower responses compared to all exposed groups.<br>CRA: Significant difference on the latency scores between the control and the exposed groups; the group differences were not clinically meaningful.<br>Interrupted speech: The mean scores were not significantly different between the groups; significant correlation was seen in the groups exposed to styrene between the cumulative exposure and the lower score in the test.<br>Speech recognition in noise: There was a highly significant effect of group on the S/N ratio; significant results were also found for all exposed groups when compared to normal reference values; the results were correlated to the current noise exposure | PAS and CANS (styrene affects the auditory system even when the exposure levels are low; the effect of a mixture of solvents on the auditory system appears to occur both at the end organ level as well as in the nervous pathway) |

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| Reference | Study design/Population/Exposure | Auditory tests/results | System affected/Conclusions |
|---|---|---|---|
| Fuente and McPherson[38] | Cross-sectional study<br>- 30 workers exposed to solvents from a paint factory; noise levels above 85 dBA.<br>- 30 control subjects | PTA: Means for thresholds for both groups were equal or better than 20 dB HL.<br>HINT: Statistically significant differences between the control and study groups for HINT SRT, HINT 1, HINT 2, HINT 3, and HINT composite.<br>RGD: Significant differences between group scores for 1,000, 2,000, 4,000 Hz, and clicks subtests; control group—lower (better) thresholds than the exposed group.<br>FS: Exposed subjects had significantly lower scores than control subjects | CANS (a possible auditory processing disorder may be related to solvent exposure) |
| Fuente and McPherson[28] | Cross-sectional study<br>- 50 workers; xylene, toluene, methyl ethyl ketone; noise levels below 85 dBA.<br>- 50 control subjects | PTA: The mean thresholds for both groups were better than 20 dB HL; exposed group—significant worse hearing thresholds at 1, 2, 3, and 6 kHz (RE) and at 1, 2, and 3 kHz (LE).<br>HINT: Statistically significant differences between the groups for HINT SRT, HINT 1, HINT 2, HINT 3, and HINT composite; controls showed better results.<br>DD, FS, and PPS tests: The exposed group—significantly lower scores than control; significant differences between right and left ear scores for the DD in the exposed group.<br>RGD: The control group obtained significantly lower (better) thresholds at 1,000, 2,000, and 4,000 Hz than the exposed group.<br>AIADH: Exposed workers had lower scores than nonexposed workers | PAS and CANS (subjects exposed to solvents may acquire an auditory processing disorder and thus the sole use of pure-tone audiometry is insufficient to assess hearing in solvent-exposed populations) |
| Keski-Säntti et al[46] | Case–control study<br>- 86 occupational chronic solvent encephalopathy patients exposed to toluene, xylene, white spirit, and industrial alcohols.<br>- 2 control groups | P300: Patient group—amplitude was significantly smaller compared to the others; the latency was longer compared to the laboratory control group, but did not differ from the matched control group; 30% of the latencies in this group and 26% in the matched controls was classified as | CANS (the decreased P300 amplitudes in occupational chronic solvent encephalopathy patients may reflect solvent-related pathophysiology; the |

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| Reference | Study design/Population/Exposure | Auditory tests/results | System affected/Conclusions |
|---|---|---|---|
| | | abnormal; the duration of exposure did not correlate with the amplitude or latency | P300 measured with the classical oddball paradigm does not seem to be sensitive at individual level or useful in clinical practice) |
| Zamyslowska-Szmytke et al[80] | Cross-sectional study<br>- 59 styrene-exposed subjects.<br>- 50 control subjects - Noise level above 85 dB A | PTA: Exposed group—significantly poorer audiometric hearing thresholds for most of the frequencies tested (86.4% had an abnormal audiogram).<br>Temporal processing tests: Significant association between exposed group and the results for the FPT and DPT tests, but not for the GIN test; styrene-exposed subjects had significantly poorer performances on the FPT and DPT than nonexposed subjects, when including hearing level and age as covariates; abnormal results for exposed group—24% for the GIN test, 59% for FPT, and 85% for DPT | PAS and CANS (results suggest an association between styrene exposure and central auditory dysfunction characterized by a temporal processing disorder) |
| Fuente et al[20] | Cross-sectional study<br>- 46 solvent-exposed subjects; toluene, xylene, methyl ethyl ketone, and varsol; noise exposure below 85 dBA<br>- 46 control subjects | PTA: Normal-hearing thresholds, but the exposed group had significantly worse thresholds at 2,000 and 3,000 Hz for RE and at 1,000, 2,000, and 3,000 Hz for LE.<br>RGD: Significant differences between groups for RGD 1,000, 2,000, and 4,000 Hz when age and hearing level were included as covariate.<br>MLD: No significant differences were observed between groups when age and hearing level were included in the analyses as covariates.<br>PPS: Significant differences between the groups for PPS right and left ear, and for PPS total score when age and hearing level were included as covariates.<br>DD: Significant differences between the groups for left ear and for total score when age and hearing level were included as covariates. | CANS (decrement in the auditory processes of binaural integration, temporal ordering, temporal resolution, and auditory closure of degraded verbal material; FS, DD, PPS, and RGD appear to be sensitive to the detection of central auditory dysfunction associated with solvent exposure) |

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| Reference | Study design/Population/Exposure | Auditory tests/results | System affected/Conclusions |
|---|---|---|---|
| | | FS: Significant differences between the groups for right ear and total score when age and hearing level were included as covariates.<br>HINT: Significant differences between the groups for speech discrimination in quiet when age and hearing level were included as covariates | |
| Keski-Säntti et al[47] | Case–control<br>- 11 occupational chronic solvent encephalopathy patients; toluene, xylene, styrene, other aromatic hydrocarbons, N-hexane, white spirit, other aliphatic hydrocarbons, perchloroethylene, trichloroethylene, alcohols, glycol compounds, ketones, and esters<br>- 13 control subjects | P300: Patient group—amplitude at Pz was significantly smaller than in the control groups; reaction time for auditory stimuli was prolonged in the patient group; the duration of exposure did not correlate with the P300 amplitude or latency | CANS (patients present slowed performance speed and difficulties in allocation of attention; occupational chronic solvent encephalopathy seems to affect posterior aspects of the frontoparietal continuity; multimodal paradigm seems promising as a tool for the clinical diagnostics of occupational chronic solvent encephalopathy |
| Quevedo et al[39] | Cross-sectional<br>- 24 gas station attendants exposed to the vapors of the organic solvents present in gasoline.<br>- 23 control subjects | TEOAEs: No significant differences between the groups. Suppressive effect of TEOAEs: No significant differences between the groups, except for the left ear, where the suppressive effect of TEOAEs was significantly higher for the control group | Auditory efferent pathway (alteration on the outer hair cells was not found) |
| Fuente et al[69] | Cross-sectional study<br>- 30 xylene-exposed participants (laboratory workers).<br>- 30 control subjects | PTA: Both groups of subjects presented with grand mean pure-tone hearing thresholds within the normal range (equal or better than 25 dB HL). Exposed group had significantly worse audiometric hearing thresholds at 0.5, 1, 2, 3, 4, and 8 kHz for the RE and at 0.5, 1, 3, and 6 kHz for the LE.<br>DPOAEs: No significant differences between groups for both ears.<br>ABR-exposed group had significantly greater latencies for wave V, I–V, and III–V interpeak latencies (IPL) for the RE; and for waves III, V, and I–V IPL for the LE. | PAS and CANS (xylene may induce in humans a decrement in PTA thresholds as well as in some CANS functions such as temporal ordering, binaural integration, and speech perception in noise) |

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| Reference | Study design/Population/Exposure | Auditory tests/results | System affected/Conclusions |
|---|---|---|---|
| | | MLD: No significant differences between the groups.<br>PPS and DD: Exposed group had significantly worse results.<br>ATTR: No significant differences between the groups.<br>HINT: Significant differences between the groups were found for HINT composite; but no significant differences between the groups were found in HINT speech reception threshold | |
| Fuente et al[16] | Cross-sectional study<br>- 72 solvent-exposed workers; methyl ethyl ketone, toluene, xylene, and Stoddard solvent, benzol, esters, and alcohols were used in the factories<br>- Noise below 85 dBA in the workplace<br>- 72 control subjects | PTA: The mean of thresholds was within the normal range in both groups; the exposed group had significantly worse thresholds (1, 2, and 3 kHz—RE; 1, 2, 3, and 8 kHz—LE).<br>TEOAEs: Exposed group had significantly lower S/N in both ears.<br>RGD: Exposed group had significantly poorer results for all RGD subtests.<br>HINT: Exposed group had significantly poorer results for HINT SRT, HINT 1, HINT 2, and HINT composite | PAS and CANS (Results provide further evidence of the possible adverse effect of solvents on the peripheral and central auditory functioning; RGD test seems to be a sensitive tool to detect central auditory dysfunction; the sole use of pure-tone audiometry is not enough) |
| Fuente et al[29] | Cross-sectional study<br>- 48 workers exposed to a mixture of solvents: toluene, xylene, methyl ethyl ketone, and Stoddard solvent.<br>- 48 control subjects | PTA: Groups presented grand mean hearing thresholds better than 20 dB HL for all the frequencies; the exposed group had significantly worse hearing thresholds (average among 0, 5, 1, 2, and 4 kHz) for the right ear.<br>RGD: Exposed group had worse results for all the RGD subtests; significant differences between the groups were found for 1, 4 kHz, and RGD clicks.<br>AIADH: Exposed group had worse results for the overall AIADH score and significantly different than the control for sound detection, speech discrimination, and sound localization/lateralization; significant slight negative correlations were observed between: the overall score of the AIADH and the RGD clicks and the overall score of the AIADH and the binaural average pure-tone threshold | PAS and CANS (the oto- and neurotoxicity induced by solvents may adversely affect the hearing performance in daily life activities; the AIADH appears to be a useful tool) |

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| Reference | Study design/Population/Exposure | Auditory tests/results | System affected/Conclusions |
| --- | --- | --- | --- |
| Chiaramello et al[31] | Cross-sectional study<br>- 7 workers exposed to styrene and noise below 85 dBA.<br>- 27 control subjects | PTA: No audiometric thresholds exceeded 30 dB HL at any frequency for the study group; all examined ears could be classified as normal or affected by very mild hearing loss only at specific audiometric frequencies.<br>TEOAEs: The interaction between frequency and groups was significant; the main nonlinear components for the exposed group are in the range of 1.5–4 kHz | PAS (difference in the amplitude of TEOAEs for the groups) |
| Juárez-Pérez et al[55] | Cross-sectional study<br>- 77 paint factory workers exposed to low levels of organic solvents mixtures and to varying noise levels (< 85 dBA).<br>- 84 control subjects | PTA: 19.5% of workers exposed to organic solvents had hearing loss in both ears; none of the unexposed workers had hearing loss. The mean hearing thresholds were significantly different in most of the frequencies.<br>ABR: The exposed group showed an increase in latencies in both ears, although they were not significant for wave I and interpeak interval III–V; adjusted for age and chronic pathologies, waves III and V, and interpeak interval latencies were significantly increased in both ears in the exposed group.<br>EHF: They mentioned that only frequencies higher than 8,000 Hz were not included in the models because most participants did not hear them, and thus more than 50% of the sample would have been lost | PAS and CANS (concurrent ototoxicity and neurotoxicity impairment in the subjects, although the solvent mixture concentrations and noise levels were low) |
| Landry and Fuente[8] | Cross-sectional study<br>- 49 workers; methyl ethyl ketone, toluene, xylene and Stoddard solvent, benzol, esters, and alcohols; noise below 85 dBA.<br>- 49 control subjects | PTA: The groups had normal hearing thresholds or sensorineural hearing loss (mean thresholds within normal range); group differences were not found for hearing thresholds for the ears.<br>DD: Significant difference between groups for the left ear—exposed group with significantly worse performance; prevalence of abnormal results for the left ear was 1.92 times higher in exposed group | CANS (Solvent exposure may be associated with a dichotic listening deficit) |

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| Reference | Study design/Population/Exposure | Auditory tests/results | System affected/Conclusions |
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| Roggia et al[60] | Cross-sectional study<br>- 53 gasoline station workers with audiometric thresholds ≤ 25 dB HL.<br>- 24 gasoline station workers with audiometric thresholds >25 < 60 dB HL.<br>- 26 control group | PTA results within the normal range; 11.7% had bilateral sensorineural hearing loss no greater than 60 dB HL in more than one test frequency; 20.8% had hearing loss only at frequencies of 6 and/or 8 kHz. The mean hearing thresholds were significantly different between groups in some frequencies when comparing subjects without hearing loss, and for most of the frequencies when comparing subjects with and without hearing loss.<br>ART: Gasoline station workers had some poorer ARTs than the controls; differences were found between the controls and the gasoline station workers with hearing loss.<br>TEOAEs: S/N ratio for gasoline station workers (even those with no hearing loss) was significantly lower than for controls for most of the frequency bands.<br>DPOAEs: Gasoline station workers had lower amplitudes at most frequencies. Gasoline station workers with no hearing loss showed significantly lower amplitudes than controls in both ears and at all frequencies tested except 8 kHz in the right ear and 6 kHz in the left ear.<br>ABR: Gasoline station workers with normal hearing thresholds: significantly longer absolute latencies in both ears for wave V than controls; gasoline station workers with hearing loss: significantly longer absolute latencies in both ears for waves I, III, and V than controls and gasoline station workers with no hearing loss; gasoline station workers with hearing loss had significantly greater III–V, and I–V interpeak latencies (IPLs) in both ears than controls and gasoline station workers with no hearing loss. Gasoline station workers with hearing loss showed significantly smaller wave | PAS and CANS (gasoline station workers have both peripheral and central auditory dysfunctions that could be partly explained by their exposure to gasoline) |

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| Reference | Study design/Population/Exposure | Auditory tests/results | System affected/Conclusions |
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| | | III amplitudes in the left ear than nonexposed subjects and gasoline station workers with no hearing loss, and they showed significantly smaller wave V amplitudes in the left ear than gasoline station workers with no hearing loss.<br>P300: No significant differences between groups for P300 latency and amplitude in both ears | |
| Sliwinska-Kowalska et al[56] | Cross-sectional study<br>- 98 styrene-exposed male workers from a plastic factory<br>- 111 noise-exposed male workers from a dockyard and metal factory<br>- 70 white-collar male workers exposed to neither noise nor organic solvents (control group) | PTA: Styrene exposure was significantly associated with poorer pure-tone thresholds (1–8 kHz); a modest effect of styrene exposure, controlled for age and mean lifetime noise exposure, was observed on hearing thresholds (1–8 kHz) in both ears.<br>EHF: A measurable threshold at 16 kHz was significantly present in control group participants as compared to noise-exposed and styrene-exposed participants. Noise-exposed participants showed a significantly low presence of a measurable hearing threshold at 16 kHz in both ears as compared to the other two groups.<br>DPOAEs: Styrene-exposed subjects showed significantly lower (poorer) amplitudes than controls; Styrene exposure seems to be associated with a narrower range of frequencies (5–6 kHz) than noise exposure (3–6 kHz).<br>ABR: Styrene-exposed workers: wave V latency around 0.12 ms earlier than controls in the both ears; significance was found only for the control/styrene contrast | PAS (The results of the DPOAE and ABR procedures suggest that styrene exposure is likely to be associated with cochlear dysfunction in humans. DPOAEs can be used to monitor hearing along with pure-tone audiometry in styrene-exposed workers) |

Abbreviations: ABR, auditory brainstem response; AIADH, Amsterdam Inventory for Auditory Disability and Handicap; ART, acoustic reflex thresholds; ATTR, Adaptive Tests of Temporal Resolution; CANS, central auditory nervous system; CRA, cortical response audiometry; DD, Dichotic Digit; DPOAE, Distortion Product Otoacoustic Emissions; DPT, Duration Pattern Test; EHF, extended high-frequency audiometry; ERP, evoked-related potentials; FPT, frequency pattern test; FS, filtered speech; GIN, Gaps in Noise test; HFA, high-frequency audiometry; HINT, Hearing in Noise test; LE, left ear; MLD, masking level difference; PAS, peripheral auditory system; PMTF, psychoacoustical modulation transfer function; PPS, pitch pattern sequence; PTA, pure-tone audiometry; RE, right ear; RGD, random gap detection; SOAE, spontaneous otoacoustic emissions; TEOAE, transient-evoked otoacoustic emission.
Note: The studies were arranged by date.