Audition and exhibition to toluene - a contribution for the theme

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Summary

Introduction: With the technological advances and the changes in the productive processes, the workers are displayed the different physical and chemical agents in its labor environment. The toluene is solvent an organic gift in glues, inks, oils, amongst others.

Objective: To compare solvent the literary findings that evidence that diligent displayed simultaneously the noise and they have greater probability to develop an auditory loss of peripheral origin.

Method: Revision of literature regarding the occupational auditory loss in displayed workers the noise and toluene.

Results: The isolated exposition to the toluene also can unchain an alteration of the auditory thresholds. These audiometric findings, for ototoxicity the exposition to the toluene, present similar audiograms to the one for exposition to the noise, what it becomes difficult to differentiate a audiometric result of agreed exposition - noise and toluene - and exposition only to the noise.

Conclusion: The majority of the studies was projected to generate hypotheses and would have to be considered as preliminary steps of an additional research. Until today the agents in the environment of work and its effect they have been studied in isolated way and the limits of tolerance of these, do not consider the agreed expositions. Considering that the workers are displayed the multiples agent and that the auditory loss is irreversible, the implemented tests must be more complete and all the workers must be part of the program of auditory prevention exactly displayed the low doses of the recommended limit of exposition.

Keywords: noise, occupational, toluene, hearing loss, noise-induced, workers.

Resumo

Introdução: Com os avanços tecnológicos e as mudanças nos processos produtivos, os trabalhadores estão expostos a diferentes agentes físicos e químicos em seu ambiente laboral. O tolueno é um solvente orgânico presente em colas, tintas, óleos, dentre outros.

Objetivo: Comparar os achados literários que evidenciam que trabalhadores expostos simultaneamente a ruído e solventes têm maior probabilidade de desenvolverem uma perda auditiva de origem periférica.

Método: Revisão de literatura a respeito da perda auditiva ocupacional em trabalhadores expostos à ruído e tolueno.

Resultados: A exposição isolada ao tolueno também pode desencadear uma alteração dos limiares auditivos. Estes achados audiométricos, por ototoxicidade a exposição ao tolueno, apresentam audiogramas semelhantes ao por exposição ao ruído, o que torna difícil diferenciar um resultado audiométrico de exposição combinada - ruído e tolueno - e exposição apenas ao ruído.

Conclusão: A maioria dos estudos foi projetado para gerar hipóteses e deveria ser considerado como passos preliminares de uma pesquisa adicional. Até hoje os agentes no ambiente de trabalho e seus efeitos têm sido estudados de maneira isolada e os limites de tolerância destes, não consideram as exposições combinadas. Considerando que os trabalhadores estão expostos a múltiplos agentes e que a perda auditiva é irreversível, os testes implementados devem ser mais completos e todos os trabalhadores devem fazer parte do programa de prevenção auditiva, mesmo expostos a baixas doses do limite de exposição recomendado.

Palavras-chave: ruído ocupacional, tolueno, perda auditiva provocada por ruído, trabalhadores.
INTRODUCTION

With the technological advances and the changes in the productive processes, the workers are displayed daily the different physical and chemical agents in its labor environment, which - in one number significant of situations - finishes for being to revert at risk to the health. This picture is presented still more unsafe when the prevalence of these risks turns it agreed exposition of these products to the noise.

In the last few decades, the occupational auditory losses have been argued in scientific publications, constituting a problem of important health in our society. However, studies appear on other agents, beyond the presence of the noise in environments of work of innumerable productive processes, that agreed, represent a potential risk to the hearing (1).

Amongst main ototoxic chemical composites, can be detached metals, suffocating and the solvents, considering this last group, most present in the half industrials. The toluene is solvent an organic present in glues, inks, oils, amongst others, and its evaluation in the labor environment is through its urinary bioindicador (examination of acid hippuric) (2).

In this article, we will present studies of the effect combined between noise and toluene, in intention to extend the knowledge how much to the effect of the concomitant exposition between the solvent and noise.

REVISION OF LITERATURE

The human being exposition to the toluene occurs from the occupational use, in the domestic environment, through the inhalation with abuse ends and of the ambient exposition. The biggest source of ambient exposition to the toluene is the production and use of the gasoline. Great amounts of toluene are introduced in the environment annually through the use of the gasoline and the production and processes of oil refinement. To calculate the levels of exposition human being proceeding from air, the ground and the water can be difficult (3).

In the last few decades, the occupational auditory losses have been argued ostensive in the half academic for the fact, unquestionable, to consist in a problem of important health in our modern society. However, more recent studies disclose that the presence of chemical agents, in association to the noise make to boosting the loss of hearing in the work environment (1).

The adverse effect of organic solvents in the health had been described in many studies (4, 5, 6). The decreases or moderate concentrations in air, organic solvets can cause temporary symptoms as euphoria, migraine, and vertigo (7, 8) whereas, in raised levels more can lead the cardiovascular anesthesia, problems and illnesses of the respiratory ways (6). The exposition of long stated period can still cause damages for the Central Nervous System as Cognitive Deficits and Emotional, what it would harm good a practical of the worker in its occupational environment, exactly that in simple tasks (9).

The toluene is a aromatically hydro-carbon, liquid and colorless, with characteristic odor, derivative of the tar of the mineral coal and the oil, used as solvent for inks, in the production of explosives, dyestuffs, medicines and detergents and as solvent industrial for rubber and oils and still in the production of other chemistries (10). It is widely used in the graphical industry. It is one of the components of the glue of shoemaker and the gasoline. This last one corresponds the main source of atmospheric emission and exposition of the population in general.

The Toluene is a solvent used of ample form in processes of anthropic transformation, particularly as solvent. In this condition, the related aromatically chemical product can, given to the degree of volatileness in conditions standard of temperature and pressure - 25ºC and 1atm - to arrive bigger impacts to the human being, revealed in the form of irritation of the skin and the mucosa. The acute effect of the toluene are similar those derive from the ethanolic poisoning, propitiating a picture of stimulation followed of depression of Central Nervous System (SNC). Already in situation of chronic exposition the risks are of hepato-toxicity, nephrotoxicity and auditory loss (5, 11).

The mechanisms of action of ototoxic substances cause functional damages or cellular damages in the internal ear, mainly in the final structures of the hearing and balance, acting first to the level of the cerebral trunk or in the auditory ways central offices (12).

When is about the auditory loss properly said, the characteristics of the audiometric curve of a attacked patient of exclusive exposition the noise or of another one, with confirmed diagnosis of otoxicity are sufficiently similar. This because both the pictures are of sensorineural origin, denote cochlear injuries, tend to be irreversible, high frequencies attack initially (acute sounds) and almost always are bilateral (2).

The ototoxic effect of the chemical agents - and amongst these, of solvent the organic ones - has configured in subject of inquiry of great number of researchers.
The NIOSH identified the emergent necessity to establish safe limits for agreed chemical substance exposition and noise (13). European consists of Directive 2003/10/EC that establishes requirements of minimum security in the health of displayed workers the risks, that the employer will have simultaneously to give to particular attention for displayed workers the chemical agents and noise, when leading in account the risk evaluation (14).

The bridge most significant of available literature on the effect of the Toluene in the Auditory System happens essentially of two origins: cases where the patients inhaled the solvent voluntarily (15) and of lead laboratorial experiments with animals. These studies evidence that the exposition to high concentrations of Toluene, for the different ways of administration (verbal, subcutaneous or inhalation) accent the auditory loss. In complementary way to this thesis, in the studies carried through in animals, it was possible to notice great synergism between this solvent and exposition to the noise.

Such conclusion is corroborated by experimental evidences with animals, where the inhalation to high levels of toluene harms the auditory system and causes loss of the audible thresholds.

**Discussion**

With the growth of the productivity and the advance of the technology, the risks of accidents and illnesses of occupational origin had increased and given origin to some harmful effect to the quality of life, to the individual and collective security of the worker.

In a study with 151 workers of the sector of rotogravure of a graphical industry of São Paulo, displayed simultaneously the noise (85-94dB) and toluene (78-390 ppm), the agreed effect of the simultaneous exposition to both was investigated the agents on the hearing and the balance (16).

In this study, using tests of hearing and balance, the workers had been divided in three groups: displayed the noise and toluene, displayed only the noise and without exposition. In the found results, the percentage of the auditory loss observed in the displayed group the two agents was significantly bigger of what in the others two groups.

Moreover, the measures of the consequence of the acoustic muscle had suggested that the joined auditory losses in this group were significantly different of the ones of the displayed group to the noise, over all with respect to probable localization of the injury. One more time here, the percentage of imperfections in the balance selection was significantly bigger in the group of workers displayed to both the agents.

Still in the same line of research, another study leads an inquiry with organic solvent and noise, observing its occupational effect. The searched individuals were all workers of rotogravure industry, of the masculine sex, with more than one year of company (17).

As mechanism of collection of data the audiometric examination and immittance testing had been used, beyond questionnaire (age, time of work, chemical time of exposition the noise and products, diabetes, hypertension, infection of ear, ototoxic medicine use, activities of leisure with noise, military service).

The workers had been divided in four groups: 50 displayed workers without any type of exposition, 50 workers with exposition alone the noise (88-97dB), 51 workers the noise (88-98 dB) and toluene (100 ppm) and 39 different displayed workers the mixture of solvent (the component greater of these mixtures was the toluene).

The results had shown to prevalence of bigger auditory loss in the group with simultaneous exposition the noise and toluene (53% in the group with exposition the noise and toluene, 8% in the group without exposition, 26% in the group with exposition only noise and 18% in the group with different exposition the mixture of solvent). In the results of the examinations of immittance testing, was met conscription presence, mainly in the groups of displayed workers to the noise and to the noise and toluene.

In the year of 1993, another study investigated workers displayed to an average concentration of 97ppm of solvent, that had presented absolute latencies and greater interpeaks in the waves in intervals I-III-V in the PEATE in relation to not displayed. With these data, one suggested that the alterations caused for the toluene can be situated in the region of the brainstem and auditory ways central offices. All the individuals of this study had normal audiology and absence of related symptoms the exposition the solvents (18).

In one another study with solvent and noise inside of the demanded limits, in a producing company of packings with approximately 800 employees, the presented results had not shown boosting of effect. Occurrence of auditory losses in displayed workers only the solvents had over all called the young attention and workers e with little time exposition. In this research one used of the audiometry examinations and immittance testing, and the collaborators had been separate and three groups: exposition only to the...
noise, exposition only to solvent and the agreed exposition (19).

In experiments with animals, were used diverse pairs of solvents and the incidence of the interactions of not additive ototoxic. Male rats of the race Long Evans had been used in places where doses of solvent (10% of concentration) were managed per 5 days of 8:30 16:30 hours of Monday a Friday. The effect were compared of 2 the 13 days after the exposition and the auditory function was gotten in the following week of exposition using BERA (reply of potential evoked in the brain). The solvents used had been trichloroethylene (TCE), toluene (TOL), mixing xylene (XYL) and chlorobenzenes (CBZ) and the combination was TOL+TCE, XYL+TCE, XYL+CBZ, CBZ+TOL (20).

For results these authors had gotten evidences of that the combination in way dose-additive of the ototoxic solvents in the effect of the hearing of the rats. In the study with CBZ+TOL the effect had developed throughout the week and not immediately. The threshold of the displayed group was of 10dB bigger of what in the group of control.

According to authors, exactly with the gotten results, cannot conclude that the solvents always will be agreed additively in its effect in the hearing, therefore get synergism when the toxic effect of the agreed expositions is bigger of what the addition of the observed effect.

In a study with rats with long exposition to the toluene for inhalation had presented found suggestive of injuries in the central initial system without evidences of injuries in the peripheral initial function (21).

With the objective to study the effect of the toluene in the structure and function of the Auditory System, it is applied tests of potential evoked (BERA - evaluation of the cochlea) in adult rats of the masculine sex, of changeable average weight between 450-500g, and created in laboratory. The experiment had beginning when the offspring reached the limit of 200 days of life, lasting for understood changeable interval between 3 and 4 months. Completed the sixth month of age the animals had been confined in individual boxes, isolation condition in which had been kept per the 30 days that had preceded the beginning of the experimental process (22).

After to be sedated received electrodes capable to measure their evoked potentials the rats had been submitted the changeable dosages of vapors of toluene with concentrations, respectively of 1000, 1250, 1500, 1750 and 2000 ppm, for a regular period of 6 daily hours, during five days of the week, throughout 4 months.

The gotten results had indicated that only three of the dosages of toluene that the animals had been submitted - of 1500ppm, of 1750ppm and of 2000ppm - had produced confirmed alteration of auditory threshold. The exposition to the toluene resulted in significant auditory deficit in the amplitude of the average frequency (8-24KHz) of the adult rats. The gotten result showed an alteration to cochlear, for the inhalation of the toluene and the main found was the cochlear trauma located in the way of organ of Corti (16-20 KHz) and half it for the apex (4-5 KHz).

Other authors had searched the effect of the simultaneous exposition of the toluene (2000 ppm) and of the noise (92 dB) in rats. These animals had been displayed to the toluene during 6h/day, 5 days of the week, for the period of one month. The results had shown the harmed induction of auditory, external loss hair cells and damaged stereocilia with bigger predominance in the rats displayed simultaneously to the noise and the toluene. The cochlear damage induced for the toluene or noise was caused by two different mechanisms, poisoning and mechanic (23).

With all the existing information and scientific results until then, new research had shown again to the occupational effect of the exposition of workers to solvent and the noise of an rotogravure industry, adding the calculation of the concentration of these mixtures in air and the examination of hippuric acid. 124 workers had participated of the study with solvent exposition to the mixture of acetate (mainly toluene, ethanol and ethyl) and different levels of noise. A questionnaire with all the workers were made (historical of work, psychosocial aspects, chemical medicines, health in general, exposition the noise and products), audiometry examination and immittance testing. Piss of these employees after hours of working was also harvested, for examination of hippuric acid (24).

The results of the audiometry had pointed 49% of the workers with bilateral auditory loss and the immittance testing results had suggested auditory upheaval central or to retrocochlear in the majority of the workers. The results had also shown alteration of the examination of hippuric acid in 95% of the workers. With this, worsening of the auditory loss was suggested, when the worker also is displayed to the toluene (from the data of acid hippuric) and 4 times more possibilities of auditory loss in workers with exposition the toluene and noise. The concentration of toluene in the air did not present significant relation with the auditory loss of the workers and with the results of hippuric acid.

In the evaluation of 64 rats displayed the toluene and ethanol, was divided the animals in 3 groups with exposition and a group of control. The first group was
displayed toluene vapors (1750 ppm, 6 hours per day, 5 days of the week for 4 months). As the group was displayed to ethanol (4g/kg for 4 months), which was injected way displayed gastric intubation and later in surrounding air for 6 hours; e the third group was displayed simultaneously to the toluene and ethanol (ethanol was injected before the exposition to the toluene). Examination of hippuric acid in the animals displayed to the toluene was realized. Piss was collected in 1º day and later each 4 days. No drunk or food was given to the animals during the exposition (25).

The results had shown that the auditory loss is more frequent in the exposition the toluene and ethanol of what only the toluene. Ethanol pure modifies the metabolism of the toluene. Auditory loss in the isolated exposition to ethanol was not evidenced.

The cochlea of displayed rats was also evaluated to the toluene, from the examination of Electrocochleography. The study was developed using two groups with each one 8 adult rats. The first group was displayed toluene vapors (1750 ppm) during 6h per day, 5 days of the week, for 4 months and second hand it did not have exposition (26).

After this period of exposition, was realized the examination of Electrocochleography and the results had not only shown alteration of located auditory cells in the portion of lower middle frequencies of the cochlea and in medium frequencies. Thus the lost cells of the Cochlea were concentrated in the region of low medium frequencies and suggested relation of auditory loss with the exposition to the toluene.

In one another study with transitory otoacoustic emissions evoked (EOAET) and the suppression effect, a displayed group was observed the noise and toluene, comparing with a group only displayed with the noise and one another one without exposition. Had been evaluated 140 collaborators with age enter 18–48 years with normal results of audiometric and immittance testing (27).

The prevalence of absence of answers in the EOAET in at least one of the ears was bigger in the displayed group the noise and toluene (64%) and in the displayed group only the noise (62%), that in the group not displayed (27.5%).

The prevalence of absence of the effect of suppression in the displayed group the noise and toluene was bigger (48.9%) in relation to displayed the noise (17.4%) and not displayed (7.5%).

The risk of absence of suppression in the group noise and toluene was significantly bigger when was compared with the other groups. The results suggest the existence of a neurotoxicity action of the toluene on the a hearing affecting particularly the portion to retrocochlear of the auditory way and causing a type of distinct injury of that one provoked by the noise.

In research on the effect of the surveyed noise and mixture of solvent by means of audiometry of high frequencies, was observed worse thresholds in the comparison of the auditory thresholds in the high frequencies of the displayed group the noise simultaneously and mixes of solvent. This difference was significant for the high frequencies, whereas the results of the thresholds tested in conventional audiometry had not shown significant differences (28).

Was also searched the mixture of solvent alterations in the Evaluation of the Central Auditory Processing in a group of displayed workers. 10 displayed workers to the mixture of solvent and 10 works not displayed had participated of the study, with results of audiometry and immittance testing inside of the normality standards (29).

The findings of the central auditory processing had been lower in the displayed group the mixture of solvent, suggesting that, exactly without presenting alteration in the auditory examination, diligent displayed the mixture of solvent they present difficulties with the daily questions, what was proven with the auditory alterations central offices presented in the processing test.

In the evaluation of the risk of auditory loss in workers of a displayed adhesive industry the noise and toluene, divided the workers in 3 groups: in the first group, 58 workers had been displayed the noise (78.6-87.1dB) and toluene (33.0 ppm, 107.6 ppm and 164.6 ppm); in the second group, 58 workers only displayed the noise (67.9 - 72.6dB); e in the third group, 60 workers of the administrative sector, that did not have any type of exposition, serving of group of control (30).

All had answered a questionnaire with information of health and style of life and had carried through audiometric examination. The tests had been carried through 14 hours after the ending of the day. The percentage of the auditory loss was calculated from the result of the worse ear. The displayed group the noise and toluene was subdivided in other groups, leading in consideration the level of the noise. Approximately 28% of the displayed workers the noise and toluene worked have more and 20 years. The predominance of the noise concentrations had been: sector noise and toluene: 83.9dB; sector noise 85,0 dB and 70,0 in the administrative sector. But 15% of the displayed workers the noise used EPI. The prevalence of the auditory loss was very bigger in the
group of noise and toluene (86.2%) in relation to the group displayed only to noise (44.8%) and 5% in the administrative group.

In research with expositions the inks and noise, studied painting sectors of automobiles of two companies and verified effect aggravation of the exposition the inks on the auditory thresholds of displayed individuals the noise between 81 and 85dB. The auditory losses verified in the displayed group the noise and inks was similar observed in the group only displayed the noise between 92-107dB (31).

In the evaluation of the effect of the solvent exposition the noise and on the peripheral auditory ways and central in workers of a graphical industry of Guarulhos in the period of September/2004 to August/2005, observed solvent association of the exposition of organic (gasoline, 3 n-hexane and thinner) and the alteration in the central auditory way was verified by means of the result of the test of the evoked potential auditory of long P300 latency (PEAL-P300) (32).

The research was realized with 136 workers and the prevalence of auditory losses found in the displayed group the noise and solvents (23.3%) was considerably bigger that in the others 2 groups, not displayed (8%), only displayed the noise (12.5%), only displayed the solvents (20%).

The results of the study suggest that the exposition to the noise had greater repercussion on the auditory threshold and the exposition to the solvents showed strong association with alterations in the results of the PEALL-P300.

Studies as the described before, in its majority carried through with animals created in laboratories, show to the effect of solvent the agreed exposition or not to the noise and (in this in case that, the toluene) and the different methods of evaluation of the auditory system.

All the realized analyses of association had indicated that the expositions, agreed or not, associate cases of auditory losses. The results had suggested that the exposition the high concentrations of mixtures of solvent and to the toluene in a noisy environment, can increase the risk significantly to acquire a occupational auditory loss. The results of the immittance testing had also suggested alteration of the central auditory system.

The tests of audiometry and immittance testing used in the studies are not enough to evaluate the effect of solvent to the hearing. The other used methods of evaluation, in show to the importance of a complete battery of audiological examinations for determination of the place and type to them of injury.

These other tests had shown that the ototoxic solvents damage the hair cells of the cochlea, suggesting that the toluene can damage cellular membranes selectively. The external hair cells, that facilitate the codification of the auditory information for the motor process of the cochlea, had been the targets most frequent of the ototoxic ones.

It cannot be conclude, however, if the solvents always will be agreed additively in its effect in the hearing. The infinity of products and the different concentrations hinder a trustworthy evaluation of its effect. The induced traumas for solvent would not be caused by the contamination of the fluid, but by poisoning of the fabric involving the ridge external, instead of the auditory nerve (20, 33).

The results had also suggested the existence of a neurotoxicity action of the toluene on the hearing affecting particularly the portion to retrocochlear of the auditory way and causing a type of distinct injury of that one provoked by the noise. The register of the EOAET and the analysis of the suppression effect can serve with instrument important in the precocious detention of the auditory alterations of origin to cochlear and to retrocochlear and for the elaboration of preventive actions in audiologic in work environments (27).

In Table 1, it meets description of main described articles above, in summary, on the mixture of solvent and noise.

**Final Comments**

Until today the agents in the environment of work and effect they have been studied in isolated way and the limits of tolerance of these, do not consider the agreed expositions. Considering that the workers are displayed the multiples agent and that the auditory loss is irreversible, the implemented tests must be more complete and all the workers must be part of the program of auditory prevention exactly displayed the low doses of the recommended limit of exposition. Studies on the ototoxic effect of the toluene in the occupational exposition are not conclusive yet.

It is important to remember that, as for the noise, the simple presence of the studied ototoxic agent (in the case the toluene), is not synonymous of exposition. So that some type of effect in the auditory agency occurs, the absorbed dose, that depends, among others, of the levels of concentrations in the environment and of the time of exposition, must be enough to cause the effect.
Study with rats with long exposition to the toluene for inhalation. Findings had been suggestive of injuries in the central initial system.

Nylen, P., Hagman, M., Toluene and Ethanol To evaluate the hearing without evidences of injuries in the peripheral initial function.

Johnson, AC

The ototoxic solvents damage the hair cells of the cochlea. One has suggested that the toluene can selectively damage cellular membranes for interrupting the way ATPase that differently are... and gets synergism when the toxic effect of the agreed expositions is bigger of what the addition of the observed effect.

1995 Function of the auditory system, the visual systems and peripheral nerve... Solvent article description on mixture of (including the toluene) and noise:

<table>
<thead>
<tr>
<th>Year</th>
<th>Article</th>
<th>Authors</th>
<th>Exposition</th>
<th>Objective</th>
<th>Method</th>
<th>Results</th>
<th>Conclusion</th>
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<tr>
<td>1990</td>
<td>An epidemiological study of the effects of exposure to noise and organic solvents on workers' hearing and balance</td>
<td>Minato, T.C</td>
<td>Noise and toluene</td>
<td>To investigate the effect of the simultaneous exposition the noise and toluene in the hearing and balance of workers</td>
<td>Interviews and tests of applied hearing and balance in 3 groups of workers in one Graphical Industry of São Paulo. Total: 81 workers. The hearing and the balance of a painter group of the sector of the interviewed workers (the noise 35-94dB) and toluene (42-380 ppm) had been simultaneously compared with a group of painter only exposed to the noise (65-90dB) and with one third group not exposed to the noise or toluene</td>
<td>The percentage of the auditory loss observed in the displayed group of the 2 agents were significantly bigger of what in the 2 other groups. Moreover, the measures of the consequence of the acoustic trauma had suggested that the period auditory losses in this group had been significantly all... of the areas of the displayed group the noise, with respect to probable localization of the injury. The percentage of importations in the balance selectives was significantly bigger of what in the group of workers displayed to both agents.</td>
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<tr>
<td>1993</td>
<td>Effects of occupational exposure to organic solvents and noise on hearing</td>
<td>Minato, I. et al</td>
<td>Solvent organic and noise</td>
<td>To investigate the occupational effect of the exposition organic and the noise of workers of a Graphical Industry of the mesoamerican sea and with more than 3 years of company</td>
<td>Auditory examination, inerrurance testing and questionnaire. The tests were performed in the chemical noise and press, diabetes, hypertension, infection of ear, ototoxic medication use, activities of leisure with noise, military service (Workers divided in three groups: 50 workers with lesser exposition 85dB, 50 displayed workers with exposition alone the noise (88-94dB), 51 workers the noise (88-94 dB) and toluene (300 ppm) and 39 different displayed workers the mixture of solvents (the component greater of these mixtures was the toluene).</td>
<td>Auditory: The noise and the solvent combined in the exposition had been clearly development of auditory loss in the group with this exposition. The test of TOL-59% group exposition and volume. 89% group without exposition, 29% group exposition noise, 88% group solvent exposition noise, immittance Testing: perception presence, mainly in the groups of displayed workers the noise and the noise and toluene.</td>
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<tr>
<td>1993</td>
<td>Neurotoxicity induced by exposure to toluene</td>
<td>Albane, C, Giorgianni, C, Minao, E, Brestain, R</td>
<td>Solvents</td>
<td>To evaluate workers displayed to toluene and not displayed, making use of the PEATE.</td>
<td>Examination PEATE in displayed the average concentration of 97 ppf of toluene and not displayed workers</td>
<td>Workers displayed to an average concentration of 97ppf of solvent, had presented bigger absolute latencies and interpeak in the waves in intervals I-III-V in the PEATE in relation to not displayed, suggesting that alterations caused for the toluene can be localized in the region of the brainstem and auditory way central offices.</td>
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<td>1994</td>
<td>Auditory effect provoked by the interaction between noise and solvent. A preventive boarding in audiology directed the health of the worker</td>
<td>Souza, M.T.</td>
<td>Solvents and noises</td>
<td>To evaluate solvent and displayed workers, the noise and solvent and noise (agreed exposition)</td>
<td>Group of workers displayed only the noise, only solvent and the two. Carried through audiometry and immittance. Study in a company of packings with approximately 2500 employees. Noise and solvent inside of the demanded limits.</td>
<td>Doubling of effect was not observed, however occurrence of auditory losses in displayed workers only meet the solvents (these the youngest workers were exposed with little time of exposition).</td>
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<tr>
<td>1995</td>
<td>Combined effects of ototoxic solvents and noise on the rat’s auditory system</td>
<td>Robert, CJS, Schwartz, PM, Sandqvist, U, Prytz, C, e Born, WK</td>
<td>Several pairs of solvents</td>
<td>To determine the incidence of interactions of ototoxic additives between some pairs of solvent</td>
<td>Silver was used: trichloroethylene (TCE), toluene (TOL), xylene (XYL) and chlorobenzenes (CBZ). The combination was TOL + TCE, TOL + XYL, TOL + CBZ and TCE + XYL. One used male rats of the noise Long term exposure to (90 ppm and 94-100 dB). The effect was compared with the 15 days after the exposition and the auditory function was gotten in the following week of exposition using BERA (replay of potential evoked in the brain).</td>
<td>The results had shown that the solvent used ototoxic had combined in a way dose additive in the effect of the hearing in the rats. In the study with TOL + XYL, the solvent had developed not immediately through the week... and the threshold of the displayed group was of 10dB bigger of what in the group of control.</td>
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<td>1996</td>
<td>Solvents and noise: a contribution for the theme</td>
<td>Augusto et al</td>
<td>Toluene and Ethanol</td>
<td>To evaluate the hearing of displayed rats for toluene and ethanol</td>
<td>Study with rats with long exposition to the toluene for inhalation.</td>
<td>The results suggest that the exposition to the high concentrations of toluene in a noisy environment can increase in significant way the risk to acquire one of auditory exposition and that the high noise cannot more considered being as only threat of the hearing of the workers.</td>
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<td>1993</td>
<td>Function of the auditory system, the visual systems and peripheral nerve after long term combined exposure to toluene and ethanol in rats</td>
<td>Wilken, P, Hagman, M, Johnson, AC</td>
<td>Toluene and Ethanol</td>
<td>To evaluate the hearing of displayed rats for toluene and ethanol</td>
<td>Study with rats with long exposition to the toluene for inhalation.</td>
<td>Finding had been suggestive of injuries in the central initial system without evidences of injuries in the peripheral initial function.</td>
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</table>
2006  
Toluene-induced Hearing Loss: A Mid Frequency Location of the Cochlear Lesions  
Campé, T. et al  
Toluene  
To study the effect of the exposure to toluene in the structure and function of the Auditory System, from tests of potential evoked (PE) cochlear in adult rats.

- Rats of the masculine sex had been used, created in a Laboratory of France. The rats had been in individual boxes of polyethylene, one month before the experiment. The animals had been anesthetized, with the acoustic auditory canal, in intention to exclude any alteration of external and auditory air and middle ear. Audiometric and electrophysiological tests for evaluation of the auditory potentials. The rats had been displayed vapors of toluene of 1000, 1250, 1500, 1750 and 2000 ppm, 6h per day, 5 days per week, for 4 months.

- But three values of toluene concentration (1500, 1750 and 2000) had produced a significant alteration in the results of the PE cochlear test.

- The result showed an alteration to PE cochlear, for the inhalation of the toluene for rats of the masculine sex and in the band of 7 to 11 months of age.

- The main finding was the loss of half the hair cells and inner hair cells in the middle frequency, from 16 to 20 kHz and from 4 to 5 kHz.

- The BERA was the usual examination for this experiment.

2007  
Correspondence between middle frequency auditory loss in vivo and outer hair cell shortening in vitro  
Liu, Y, Rao, D e Fechter, L.D.  
Toluene  
To demonstrate that the exposition of the toluene in vitro produces morphologic changes in the external hair cells.

- They showed in a study with 15 pigs of the Guinea, that the exposition to the toluene, with a concentration a little above of the allowed level, produces morphologic changes in the external hair cells (reduction) and a effect on the cells of the half of the apical region.

- The reduction of the cells happened in first the 15 minutes of exposition and had its apex to the 55 minutes. The basal cells (high frequency) in the portion of the cochlea had lost after about 15% of a total length of 80 minutes of exposition. According to these same authors, the external hair cells, which facilitate the codification of the auditory information for the motor process of the cochlea, are more frequent of ototoxic.

- The external hair cells are more frequent of ototoxic. They facilitate the codification of the auditory information for active the motor process of the cochlea.

2007  
Combined effects as simultaneous exposure to noise and toluene on hearing function  
Lutajé, H e Campo, P.  
Toluene and Noise  
To study the occupational effect of the exposition of workers solvent and the noise of an industry and rotogravures.

- The mixture of (mainly toluene, ethanol and ethyl acetate) and different levels of noise also Calculated the concentration of toluene in air did not present significant relation with the auditory loss of the workers and with the effects of toluene in air.

- There is a coexistence of both mechanisms to boosting the effect of the cochlea.

2007  
Toluene-induced hearing loss among rotary printing workers  
Morata, T.C et al  
Solvents and Noise  
To study the occupational effect of the exposition of workers solvent and the noise of an industry and rotogravures.

- 49% of the workers had presented bilateral auditory loss - the concentration of toluene in air did not present significant relation with the auditory loss of the workers and with the effects of toluene in air.

- The solvent noise is suggested more complex audiological examinations for the evaluation of the hearing of displayed workers and (audio tonal, vocal, immittance testing and initial tests) to avoid the auditory loss.

- The recommendation of the exposition limits the chemical products are not adjusted when more expositions exist.
Toluene Ototoxicity in Rats: Assessment of the Frequency of Hearing Deficit by Electrocochleography

Lataye, R., Campo, P., Loquet, G.

To evaluate the Cochlea of displayed rats the toluene, from the examination of Electrocochleography.

The study was developed in a laboratory on France and used 2 groups of 6 adult rat. The first group was displayed toluene vapors and second hand it did not have exposition. The animals approximately had between 50-60 g and 4 months of age. The animals of the first group had been displayed vapors of toluene of 750 ppm, during 9h on day 5 days of the week, for 4 months. Only after this period of exposition, the examination of Electrocochleography was realized.

The examination not only showed alteration of located auditory cells in the portion of lower middle frequencies of the cochlea and in medium frequencies.

The examination of Electrocochleography not only showed an alteration in the medium frequency of 16KHZ, but also in the medium frequency decrease of 4khz. Thus the lost cells of the Cochlea were concentrated in the region of low medium frequencies. Relation of auditory loss with the exposition to the toluene is suggested.

Comparison of toluene induced and styrene induced hearing losses

Lataye, R., Campo, P., Loquet, G.

Styrene and Toluene To compare the effect of the toluene and the styrene in the auditory system of rats.

96 rats with 450-500g and 4 months of age had participated of the study. One used doses of 1000-2000 ppm toluene and 500-1500 ppm of styrene (exposition of the vapor: 6 hours per day 5 days of the week, for 4 consecutive months). The auditory system was tested Pre-examinations of potentials was asked in freq of 2 - 32 Hz.

- similar results of curve, with concentration of 950ppm of toluene and 950 ppm of styrene, in freq of 12, 16, 20 and 24 Hz - the effect of the toxicity of the toluene start with concentrations of 900ppm and 50 ppm of styrene - permanent alterations in the agency of corti and cells - the two solvents have similar toxic effect

- Exposition the toluene and styrene cause permanent auditory loss in rats - The styrene has a bigger toxic effect of what the toluene - Toluene and styrene dangerous industrials for the hearing of adult rats are solvents - Hair Corti and some cells are the affected structures more - Styrene concentrations are 2 times more harmful than toluene

Toluene and styrene intoxication route in the rat cochlea

Blachere, V, Campo, P., Loquet, G. e Roure, M.

To inquiry of the route of the poisoning for which the solvent reaches the cochlea.

Use of the toluene (1750 ppm) and styrene (1750 ppm) in adult rats Long Evans for 10 hours (being consecutive 6 and 4 in the following day). The FCE (fluid cerebrospinal), blood, brains tissue, auditory nerves, WNT (hair of the internal ear) and cochlea had been analyzed in such way for the toluene how much for the styrene using chromatography for gas, giving more approach to the cerebellum and regions of bridge.

The found concentration of solvent in the brain was bigger of what the joined one in the blood. The concentration in brain was of 47,6 mg/g in brain and 50,1 mg/g in styrene blood and 45 mg/g. 1 hour after of the 4-hours of the exposition of 2000 ppm of toluene. The concentration of styrene in brain was of 88 mg/g and the blood concentration of 37,5mg/g.

The differences of ratios found in the brain and the blood, the tissue, the brain and the styrene are epipharynx and the cortical cerebro are constituted in a way by rich regions in fats, compared with the blood. The styrene is more present in the bridge and the cerebellum that are rich in fats. The toluene and the styrene chemically are not extracted by water environments.

The rate of poisoning shown in this study tells that the concentration of the Agency of Consilium have to a WAG, therefore the solvents hardly is found in rats. The authors suggest two probable routes of evoked poisoning in the reduced auditory loss for solvents. 1° the solvents would spread out of the eighth nerve for the hair cells, because the concentration of solvent is bigger in tissues that in the blood. However is difficult to explain the patologiathical standard of the damage of the auditory of Cort for the solvents (the several hair cells of the third column more are damaged of what the second column) and that it is damaged in the first one. 2° the solvents would be carried by the blood if they would spread out on the ridge external of the cochlea and would reach the cells of Remen. Hair cells are in connection with the cells of Blinder that are located on the internal hair cells, and thus the solvents reach the agency of Cort.

The induced trauma for solvent would not be caused by the contamination of the fluid, but by poisoning of the fabric involving the edge external, instead of the auditory nerve.
<table>
<thead>
<tr>
<th>Year</th>
<th>Title</th>
<th>Authors</th>
<th>Summary</th>
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<tbody>
<tr>
<td>2001</td>
<td>Displayed workers simultaneously the noise and toluene: study of the otoacoustic emissions evoked and effect of depression</td>
<td>Bernardi, A.P.A.</td>
<td>The study of the neurotoxicity of toluene on the auditory function in guinea pigs displayed workers simultaneously the noise and toluene. The prevalence of absence of answers in the EOAET in all the group is higher than in any of the other groups.</td>
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<td>2001</td>
<td>Effect of chemical products and noise in the genesis of the auditory loss</td>
<td>Andrea Pires de Mello de Andrade et al.</td>
<td>The prevalence of absence of answers in the EOAET in all the group is higher than in any of the other groups. The results suggest the existence of a neurotoxicity action of the toluene on the hearing affecting particularly the portion of intracochlear of the auditory pathway and causing a type of distinct injury that are provoked by the noise. The results of the EOAET and the analysis of the suppression effect due to noise have shown important results in the prevision of the elimination of the auditory alterations of exposure to noise and its neurotoxic effect in the auditory pathway.</td>
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<td>2001</td>
<td>Occupational toluene exposure and auditory function: results from a follow-up study</td>
<td>Schaeper, M., Demers, P., Michaud, Z., Biezakowicz, M., Sweeney, A.</td>
<td>The results have shown that, mostly, the levels of noise were above the Norma Regulator of the country (55 dB(A) - 65 dB(A)) and the concentrations of toluene were lower than the established for the reference (40 ppm). The results of the EOAET in the exposed auditory noise and the solvent were below the prefixed levels.</td>
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<td>2002</td>
<td>Effect of chemical products and noise on the auditory function in guinea pigs</td>
<td>Azevedo et al.</td>
<td>The results of the EOAET in the exposed auditory noise and the solvent were below the prefixed levels. With these results, the authors suggest that the exposure to these agents, mostly inside of the area limit, can increase the occurrence of auditory loss, being warned about the fact of Bintel of noise exposure daily and sometimes without the adequate protection.</td>
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<td>2003</td>
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<td>Low-level toluene disrupts auditory function in guinea pigs</td>
<td>Feuer, A. et al.</td>
<td>The results have shown that, mostly, the levels of noise were above the Norma Regulator of the country (55 dB(A) - 65 dB(A)) and the concentrations of toluene were lower than the established for the reference (40 ppm). The results of the EOAET in the exposed auditory noise and the solvent were below the prefixed levels.</td>
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<td>2005</td>
<td>Assessment of central auditory processing in a group of workers exposed to solvents</td>
<td>Fuente, A. et al.</td>
<td>The results have shown that, mostly, the levels of noise were above the Norma Regulator of the country (55 dB(A) - 65 dB(A)) and the concentrations of toluene were lower than the established for the reference (40 ppm). The results of the EOAET in the exposed auditory noise and the solvent were below the prefixed levels.</td>
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<td>Chang, S.J. et al</td>
<td>To evaluate the risk of auditory loss for displayed workers the noise and toluene. The workers of an adhesive industry had been divided in 3 groups: in the first group, 58 displayed workers the noise (79.6-87.7) and toluene (33.0 ppm, 110.9 ppm and 144.5 ppm) in 24 h and in the third group, 68 workers of the administrative sector. All had answered to a questionnaire with information of health and style of life and had carried out audiometric examination. The tests had been carried out 144 h after the ending of the day. The percentage of the auditory loss was calculated from the result of the ear worse. The displayed group the noise and toluene was subdivided in other groups, leading in consideration the level of the noise. Approximately 28% of the displayed workers the noise and toluene worked have more than 20 years. The predominance of the noise concentrations had been sector noise and toluene (83.6 ppm). workers of the administrative sector. All had answered to a questionnaire with information of health and style of life and had carried out audiometric examination. The tests had been carried out 144 h after the ending of the day. The percentage of the auditory loss was calculated from the result of the ear worse. The displayed group the noise and toluene was subdivided in other groups, leading in consideration the level of the noise.</td>
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<td>2006</td>
<td>Toxic solvents in car paints increase the risk of hearing loss associated with occupational exposure to moderate noise intensity</td>
<td>EL Shafy, A.</td>
<td>It was studied two painting sectors of automobiles of two companies and verified effect aggravation of the exposition on the auditory thresholds of displayed individuals the noise between 61 and 85 dB. The auditory function in the displayed group the noise and toluene (83.9 dB) was similar observed in the group only displayed. It was estimated that the noise concentrations in the group displayed the noise and toluene was 85 dB (A) for 8 h of exposition.</td>
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<td>2017</td>
<td>Thesis of Doctored USP - solvent Occupational Exposure - noise and peripheral auditory alterations and central effects.</td>
<td>Dra Alice Penna Bernardi</td>
<td>To evaluate the effect of the solvent exposition the noise and on the peripheral auditory areas and central in workers of a graphical industry. Association of the exposition of 3 organic solvents (gasoline, n-hexane and thinner) and alteration in the central auditory way by means of the results of the test of the evoked potential of auditory. The auditory thresholds of the displayed group the noise and toluene was 83.9 dB and the displayed group only the noise was 82.1-101.6 dB. The prevalence of the auditory loss was similar observed in the displayed and control group. Workers with minimum age of 50 years for the process of Presbycusis was not to intervene with the results. The prevalence of auditory losses found in solvent displayed group the noise and toluene 83.9 dB was considerably higher than in the other 2 groups. Workers with minimum age of 50 years for the process of Presbycusis was not to intervene with the results. prevalence of auditory losses found in solvent displayed group the noise and toluene (83.9 dB) was considerably higher than in the other 2 groups.</td>
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<tr>
<td>2018</td>
<td>Ototoxicity of Toluene and Styrene: State of Current Knowledge</td>
<td>Hoel, P. and Lison, D.</td>
<td>In recent years, the toxic effect of the toluene and styrene in the auditory system has been a topic of investigation. The limitation found in the study epidemiologic is the insufficient characterization of the exposition to the toluene and styrene, with also other solvents. The studies made with animal bring the internal exposition. The potential variable of absorption is different. The individual metabolism must be considered. Considering that the workers are displayed the multiples agent and that the auditory loss is irreversible, the implemented tests must be more complete and all the workers must be part of the program of auditory prevention.</td>
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</table>

Being thus, it is important that the managers and/or professionals who work with the question of the Health of the Worker, is alerted of the effect combined concerning the exposition to noise and chemical substances, so that it can search tools for quarrels of effective norms and the programs of auditory conservation, contributing for more good a management in the health of the worker. The perspective of study of the combined effects, not only of the toluene, but of the majority of the chemical agents, must deserve greater attention so that if it can plan measured adequate of protection, rethink the existing Programs of Auditory Conservation.

**BIBLIOGRAPHIC REFERENCES**


12. Morata TC, Nylén PR, Johnson AC, Dunn DE. Auditory and vestibular functions after single or combined exposure to toluene: a review. Archives of Toxicology. 1995, 69:413-43.


