

Critical Review of Extreme Effects of Exposome/ Interaction between Genetics and Environment on Hearing Disorders Reclassified

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ABSTRACT

This article has critically reviewed the literature's information on the deleterious effects of the exposome on the reclassification of auditory disorders. Thus, a theoretical framework was proposed including the conceptual model and hypotheses to be tested in the process of hearing impairment. The exposome describes the interactions between genetics, chronobiology, diet, risk behaviour, infections, urbanization, physical environment, active smoking, epigenetics, health system, biometrics and reclassification of the host man's auditory disorders.

Conclusion: With the progress of science, the genesis and development of hearing disorders (mixed or isolated by conduction and perception) are currently elucidated by the exposome (integration of the environmental harmful exposure set, infections, and oxidative stress during the evolution of age.

Keywords: Exposome, Genetics, Environment, and Deafness.

INTRODUCTION

The context relates to the situation of hearing disorders worldwide (1), in Africa, in developing countries [1] and in the city Kinshasa Province (VPK), Democratic Republic of Congo (DRC), part of Central Africa. [1]

The World Health Organization (WHO) considers hearing disorders, concepts of severity-progression: less severe disabling hearing loss and deafness, profound progression of disabling hearing loss. [1, 2]

Incapacitating hearing loss and deafness according to chronobiology (advancement in childhood age through adulthood to senescence/senility (against the term aging) worldwide: disabling hearing loss in children (hearing loss greater than 30

dB to tonal audiometry), [1,3] with 60% of cases where 34 million among the 466 million people in the world including adults (hearing loss greater than 40 dB in the best ear) in the world. [2, 3]

With the progress of science, the genesis and development of hearing disorders are currently elucidated by the exposome (integration of the set of harmful environmental exposures including active or passive smoking, the various pollutions of which particles and noise nuisance, infections, behavioural and occupational exposures, the interaction between genetic and environmental factors). [3]

Epigenetics (Interface between environmental, ecotoxic and genomics-mutation factors); [3] from birth to adulthood in a personalized approach (predictive, early

diagnosis, and scientific therapeutic follow-up biomarkers), [4] and not to mention the interaction between environmental, genetic-host factors and psychological factors to be controlled by a holistic approach. [5]

Also the causes of hearing problems can be:

- congenital birth (from fetal life to birth): (hereditary genetic factors or complications during pregnancy or childbirth related to low birth weight, rubella, asphyxia at birth, inappropriate use of medicines (aminoglycosides, antimalarials, diuretics, Icter and HIV; [2, 3])
- acquired at any age of chronobiology (infections including meningitis, measles, mumps, chronic ear infections, head trauma, explosions (machine noise, earphones, earplugs or a body and sensory cell degeneration. [2])

Hearing disorders cause functional impacts (decline in the ability to communicate with others, delay in acquiring spoken language often overlooked in childhood). [2] Social and emotional aspects (impacts on daily life, feelings of loneliness, isolation and frustration among the elderly) [2, 5] and economic aspects (annual cost of US\$750 billion) related to the care of hearing loss or hearing loss regardless of the cost of hearing aids with lost productivity. [6-8]

In the diagnosis of the types of hearing disorders, voice acoumetry in a less rich environment and more accurate introductory tonal audiometry in a rich environment reveal a complete or partial loss of one or more two ears classified as mild, moderate, and severe or deep. [7] These hearing losses are also classified as transmission deafness and sensorineural or sensorineural deafness. [2, 8]

1. Theoretical Framework

The theoretical framework of the study includes the conceptual model and the hypotheses to be tested:

1.1 Conceptual Model

The conceptual model of this study was based on five diagrams (Figure 1- Figure 5) using mathematical equations (Modeling) of a process with dependent variables (hearing disorders: prevalence, together and classification of hearing disorders, incidence of severe-deep deafness and deaf-blindness) and independent or explanatory variables (covariable, interactions, interface and colinearity: genetic factors, factors ethnic-military crisis-conflicts, ecotoxics, chronobiology) Sociopolitique

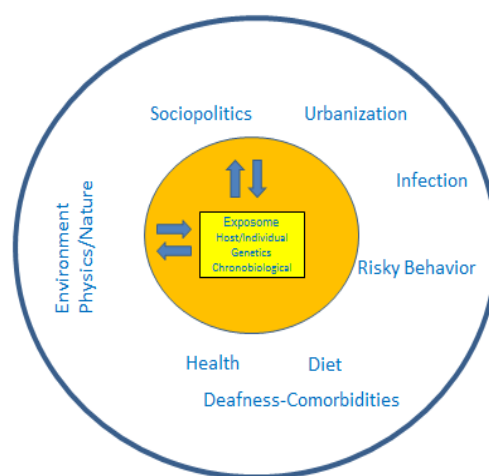


Figure 1. Exposome diagram: circle of individuals exposed to different environments of the peristase.

Figures 1 and 2 define the exposome explaining the interaction between environmental factors (physical agent, climate change/climate variability - El Nino - La Nino, socio-political crises, cahotic urbanization/urban-rural peripheral extension of the eastern region of Kinshasa (Houyoux), risky lifestyle behaviours (alcoholism, smoking, diet, level of health system) and personal factors are not Sex, age through DNA and RNA alterations to develop hearing disorders.

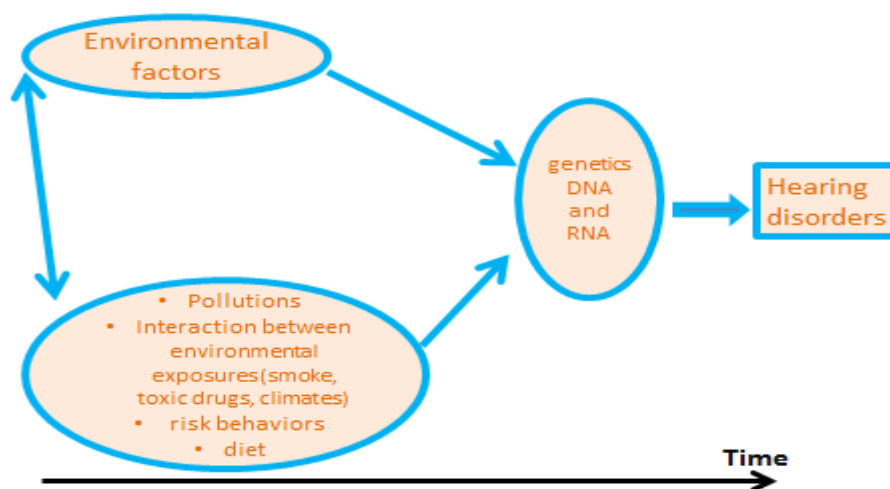


Figure 2. Exposome diagram: genetic factors, environmental factors of peristasis and hearing disorders.

Graph of cybernetic-connected arrows from the left (environmental factors) through intermediate mechanisms to the far right with independent variables under the impact of precise or unsted time. The process was explained by the exposome with the individual at the center, and the environmental factors at the periphery (Figure 1-2) and the interface between the environmental factors of the peristosis and the genetic factors (Monogenemie, polygenemia) of Individual (Figure 3).

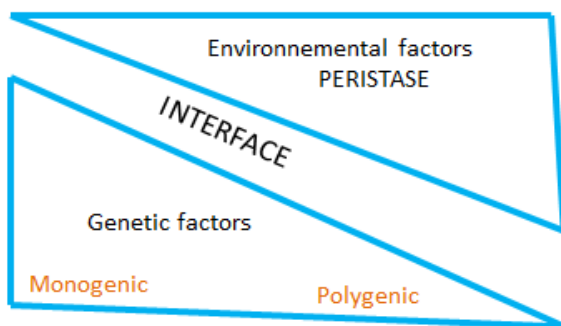


Figure 3. Epigenetics.

Indeed, the environment encompasses the Individual (Personalized Medicine, Oto-Rhino-Laryngological Health/Surdity-Comorbidity, Diet, Infections, Risk Behaviours and Pollution).

Deafness (dependent distal variable) will be explained by different independent variables (tobacco, chronobiology, mutation, occupational exposures, ecotoxicity, drugs, genes, sex, Y chromosome, genity, genotype, blood type); in the extreme the intermediate mechanisms

in the middle of the process (Inflammation, endothelial dysfunction, oxidative stress, mutations, toxicity).

On the other hand, and in light of the reclassification of hearing disorders (transmission deafness, neurosensory deafness/severity), the thesis becomes an organization of basic research (basic sciences including anatomy, physics, immunohistochemistry, molecular biology, pathophysiology, pharmacology, tobaccoology, anatomopathology), ENT clinical research (acoumetry, audiometry, physical examination), epidemiological (environmental, ecotoxicology) and molecular (oxidative stress) to become involved in a spiral of early and accurate diagnosis of auditory disorders for prognosis/severity in personalized therapy, therapeutic follow-up/ follow up monitoring and primary, secondary, tertiary and fourth-year prevention in a single health [2,3]; the same thesis with its reliable results to improve the promotion of ENT health and the prevention of hearing disorders in Hospitals in Kinshasa.

In addition, there are two-way implications between hearing disorders (dependent and independent variables depending on the nature/types of studies: cross-sectional studies for time-free prevalence, control case studies (only retrospective study) with the arrow starting from density of the dependent variable left to independent variables without time

implication) and prospective or interventional studies with left-handed arrow with variables density with no time/duration impact (Figure 4). The constant, the analogy (reversibility, significant statistical association).

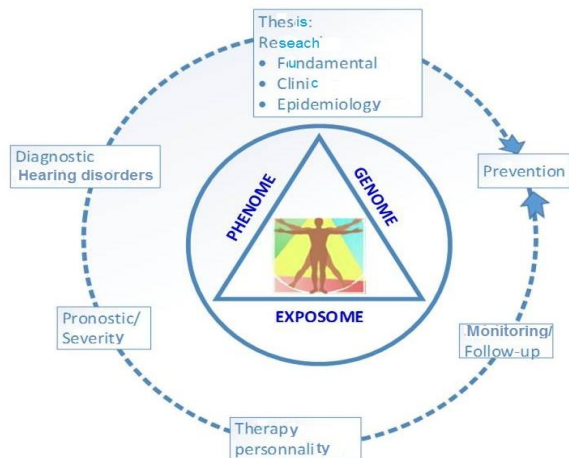


Figure 4.Reclassification of hearing disorders.

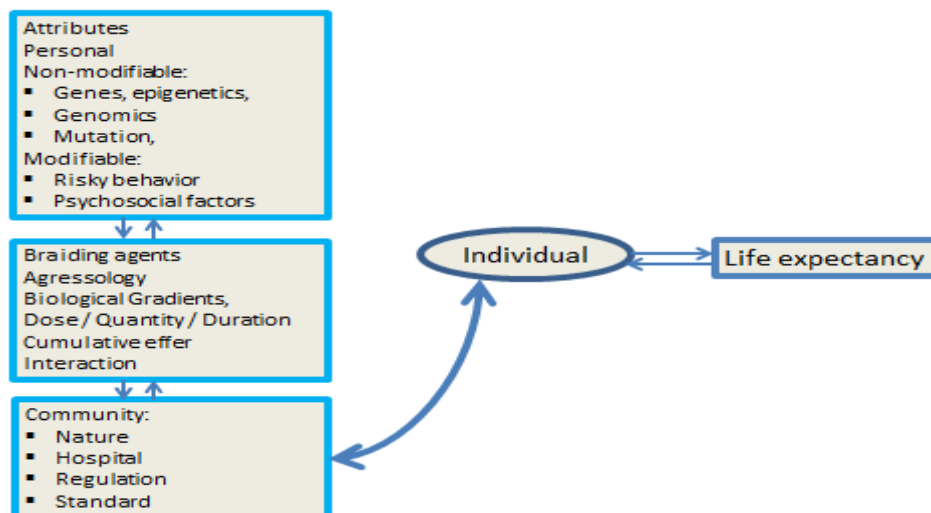


Figure 5.Understanding two-way interactions in process development.

1.2 Hypothesis

Biostatistically, the null hypothesis and the alternative hypothesis have been considered, but the assumptions in this study have also been formulated as follows:

- there is a prevention of epidemic-looking deafness in School environment in the city of Kinshasa; sensorineural deafness is more severe-deep than transmission deafness;
- there is an excess risk of sensorineural deafness >50% (OR -1-0.5) in individuals with exposure to congenital

The biological gradient (quantity, duration, cumulative effect of toxicological, dietary sound exposures) and stratification of independent variables by gender or age advancement, residence, origin of province (ethnicity) and multivariate analyses will be considered to eliminate biases and confounding factors.

Indeed, the support associated with intermediate mechanisms constitutes the pillar of the initiation of factual realization (evidence-based evidence or evidence based medicine), the involvement of family members, health professionals and the community (participatory medicine) and thesis management.

causes, age <50 years, active smoking, passive smoking, oxidative stress, metabolic syndrome-atherosclerosis, comorbidity, inflammation, virus (CMV), Helicobacter Pylori, antibiotics, allergy, job's syndrome, nutrient deficiency, iron, hypovitaminosis D, toxoplasmosis, measles, low birth weight, double nutritional burden, socioeconomic level/ Acculturation.

2. TABAGISM

2.1 Botanicals, origin and history

Tobacco is a plant (Nicotianatabacum) native to Fie-Je Tobago, a small island in northern South America. It is a product made from the leaves of tobacco; dried and variously prepared, they smoke, take or chew. [9] It is a plant of the family of solanaceae, families of gametopetal plants, the class of angiosperms and the branching of phanerogame plants. [10] Christopher Columbus discovering America in 1492 finds that Indians use tobacco for its magical and medicinal properties. In honor of Jean Nicot, the tobacco is called "Nicotianatabacum" which is the main variety, the genus being Nicotiana. It was at the end of the 20th century that the word tobacco appeared. [11]

2.2 Composition of Tobacco Smoke

The composition of tobacco smoke was highlighted through the study of smoking markers. The marker of smoking is any substance or metabolite of a substance initially present in cigarette smoke found and dosed in certain biological environments of an individual.

2.3 Measuring Exposure to Smoking

Exposure to Passive Smoking can be measured by:

- measuring devices set in a room or by the use of portable system by a non-smoking subject who is willing to experiment.
- by taking air around exposed non-smokers Biological monitoring by measuring compounds of tobacco smoke in the blood, saliva, urine or hair of the exposed person. [12]

The main interest of markers is to be able to quantify tobacco exposure in an objective way. There are two types: Specific Markers and Nonspecific Markers.

2.2.2 Specific markers of tobacco exposure

Are found only in exposed smokers and non-smokers. This is nicotine (short half-life 2 to 4 hours) because quickly metabolized and its metabolite cotinine (long half-life), (19-72 hours). Cotinine can be measured even on the subject that has

been removed from the smoking mood. [12, 13] Because of its long half-life, the dosage of cotinine is the most achieved. This dosage is done in the blood, urine, saliva and hair by radio immunological dosage or chromatography in the gas phase. A serum rate of 2.5 ng/ml is very significant or higher. This cotinine measured in the hair is then a reflection of a longer exposure and then that a centimeter of hair corresponds to 1 month of exposure. However, these dosages are not carried out routinely. [12, 13]

2.2.3 Non-specific tobacco exposure markers

- ✓ Carbon monoxide: is the incomplete combustion product of tobacco. It belongs to the gaseous phase of tobacco smoke and is found in the primary current. It is released by other sources of the indoor environment such as stoves, radiators and can come from outside because of exhaust gases.
- ✓ Thiocyanates: are a reflection of 15-day exposure with a long half-life but measurements are disrupted by drug and food interactions. It is measured in blood, urine or saliva.
- ✓ Cadmium (bioaccumulating heavy metal)
- ✓ Protein or DNA adducts resulting from exposure to tobacco smoke, measured in blood or urine. [12]

2.2.4 The smoke cycle

Tobacco smoke enters the body through issues such as the oral cavity, nasal cavities and ear canals. Whether it is its front door, tobacco smoke passes through the trachea via the pharynx (aerodigestive crossroads) to end up in the lungs.

During hematoma, this smoke passes through the alveolo-capillary barrier to the bloodstream. From there, carbon monoxide binds to hemoglobin with a greater affinity than oxygen to form the short half-life carboxyhemoglobin of 4 to 6 hours. This carbon monoxide is eliminated in exhaled air. Some of this smoke is also absorbed by the nasal and oral mucous membranes. [11]

Thus, tobacco smoke acts directly or indirectly on almost all organs either by the

direct action of its irritants on the airways, or by the passage of certain products into the blood. [14]

Smoke currents

It is customary to distinguish three aspects of cigarette smoke, called currents: the so-called primary current is the one that is breathed by the active smoker, the secondary current is the one that is inhaled by non-smokers exposed to an atmosphere smoking the tertiary current is one that is exhaled by the active smoker. [12]

Environmental smoking is a priority for smoke that escapes from the pyrolysis beak of cigarettes. For a cigarette, the duration of the secondary current is much longer than that of the primary current. The concentration of most substances present in the secondary current is at the time of their emission at much higher concentrations than the primary current. This is the case for the CO and CO₂ gas component, carcinogens, irritants and also nicotine. [15]

The very high concentrations of these substances at the time of emission drop very significantly in the ambient air, depending on their volume of distribution in a space and the ventilation of the premises. The passive smoker will therefore inhale a gas flow in which these products are certainly present but at varying concentrations. The cramped containment of residential, professional or recreational areas is often accentuated by thermal insulation and lack of ventilation.

The importance of smoking in the population means that each of us is in a variety of ways, a passive smoker. [15, 16] The main stream smoke is little diluted (40 ml of smoke in 600 ml of a resting breath). The smoke from the lateral current, whether inhaled by the smoker himself or his entourage, is very diluted, but the exposure time can be very long. Starting in infancy, this exposure period can be very important. [15]

A resting man breathes 12 times per minute, or $24 \times 60 \times 12 = 17280$ breaths per day possibly containing second-hand tobacco smoke in a smoky room. A smoker who

smokes 2 cigarettes per day, taking 14 puffs per cigarette will take 280 breaths containing smoke from the main stream (or 1.6% of the day's breathing cycles). For the assessment of exposure to respiratory pollutants: 2 types of measures are taken into account.

- For professional exposure, an exposure of 8 hours per day of work for 40 years is considered or 50 million inspirations (double or tripled if the work is physical work).
- For the general exposure of the population, calculations will take into account 24 hours of exposure per day over 70 years or 400 million inspirations. [12, 16]

The duration of exposure to second-hand smoke (number of years and number of hours during the day) is often much longer than for active smoking; it starts in early childhood and can be more than 12 hours a day, adding up in some adults, professional smoking exposure, home exposure and exposure during free time.

2.3 The mechanism of the deleterious effects of tobacco

The mechanisms of the deleterious effects of tobacco are numerous and intertwined: mucous irritation, increased mucous permeability, decreased migration of macrophages and polynuclear neutrophils, an increase in total serum IgE. [13, 17, 18]

- The pathophysiological mechanisms linking smoking exposure and pathologies are paradoxically still poorly known, especially those concerning the immune system and even more those involving the mucous immune system;
- At the level of systemic immunity, tobacco exposure induces an acquired immune deficit at least partially that can promote the development of hypersensitivity phenomena and autoimmune pathology.

As for the mucous immune system, exposure to tobacco smoke induces abnormalities of innate immunity as well as adaptive immunity to which are added local

inflammatory phenomena. [18] At the ent and stomatological spheres, tobacco induces inflammatory states and reversible alteration of the olfactory and taste sense. [11]

The health effects of passive smoking are important and well described in children: more common ENT and gastroenteritis infections: Nicotine stimulating the secretion of gastrin and motor activity of the intestine. [19] Neuropsychic effects: nicotine attaches in seconds to the brain's nicotinic receptors, promotes intellectual concentration and memory, has an anxiolytic or even euphoric but short-lived action. As most additives do, it indirectly increases the activity of mesolimbic dopamine neurons by stimulating nicotinic receptors on dopamine cell bodies located in the area ventral tegmental. This stimulation increases dopaminergic activity mainly in DA neurons that project on the nucleus accumbens or causes sensations of pleasure phenomena responsible for pharmacological dependence. [20,21]

Absorption: Cigarette smoke, especially blond tobacco smoke, has an acidic pH. This does not allow the resorption of nicotine by the oral mucosa but on the other hand very easily by the lining of the bronchial epithelium and alveoli; very rapid resorption due to the large area; role of deep inhalations in search of a nicotine shoot. This bronchial inhalatory practice leads to numerous Malpighian metaplasias and thickening of the normally unicellular epithelium. [20,21]

In the long term, exposure to other people's tobacco smoke is associated with an increase in coronary and myocardial infarction of about 30% and an increased risk of lung cancer of more than 40%.

Conflict of interest

The authors declare no conflict of interest.

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Authors' contribution Study design:

- Study design and writing: SG, BLM.

- Scientific advice: TA, MM, LB.

Analysis and interpretation of data: NNA

Writing of the final manuscript: SG, MNR, MMM, MTC.

All authors approved the final and revised version of the manuscript

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