Monitoring Vibroacoustic Disease

Nuno A. A. Castelo Branco, Augusto J. F. Martinho Pimenta,

José M. Reis Ferreira, Mariana Alves-Pereira

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***Abstract*—Vibroacoustic disease (VAD) is a consequence of long-term (years) exposure to low frequency noise. Since the early 1980's, the ongoing attempt has been to find a non-invasive and reliable diagnostic tool that could simultaneously monitor the evolution of VAD with accuracy. Initially, neurophysiological tests were used, but as the cardiovascular pathology of VAD became evident, echocardiography became the diagnostic tool of choice. Despite the non-invasiveness and the availability echocardiography, the subjectivity of measurement induced by techinicians has deemed it inadequate. Recent evidence indicates that pulmonary function evaluations could provide answers for an accurate and inexpensive tool to monitor VAD.**

***Index Terms*—echocardiography, epilepsy, low frequency noise exposure, pulmonary function tests.**

I. Introduction

VIBROACOUSTIC disease (VAD) is a whole-body pathology caused by excessive exposure to low frequency noise (LFN) (?500 Hz, including infrasound) ?1?. Initially identified among aeronautical technicians, VAD has also been observed in military ?2?and commercial pilots ?3?and aircrew, and in a civilian population exposed to environmental LFN ?4?. Other individuals who were unsuspectingly exposed to LFN have also been identified with VAD ?5?.

LFN exposure induces an abnormal growth of extra-cellular matrices. This is reflected by abnormal thickening of cardiovascular structures ?6?, ?7? and by the appearance of pulmonary fibrosis that has been replicated in LFN-exposed rodents, under laboratorial conditions ?8?-?11?. LFN has also been identified as a genotoxic agent in both LFN-exposed workers ?12?, ?13? and animal models ?14?, ?15?. All lung tumors in VAD patients (7 smokers/3non-smokers) are of the same type of cellularity – squamous cell carcinomas ?10?. In fact, all other respiratory tract tumors (2 glottis 1 smoker/1 non-smoker) are also squamous cell carcinomas. Through electron microscopy, rats exposed to LFN exhibited squamous metaplasia ?11?.

The appearance of symptoms depends on the number of years of occupational exposure, as Table I indicates ?1?. There is a neuro-psychiatric picture that initially involves humoral and behavioral changes: mood swings, increased irritability and aggressiveness, and memory disturbances that are mostly reported by family and friends.

Table 1. Data corresponding to a group of 140 aircraft technicians (selected from an initial group of 306 workers), occupationally exposed to LFN. Exposure time refers to the amount of time it took for 70 individuals (50%) to develop the corresponding sign or symptom ?1?

Clinical Stage	Sign/Symptom
Stage I- Mild (1-4 years)	Slight mood swings, Indigestion & heart-burn, Mouth/throat infections, Bronchitis
Stage II- Moderate (4-10 years)	Chest pain, Definite mood swings, Back pain, Fatigue, Fungal, viral and parasitic skin infections, Inflammation of stomach lining, Pain and blood in urine, Conjunctivitis, Allergies
Stage III – Severe (> 10 years)	Psychiatric disturbances, Haemorrhages of nasal, digestive and conjunctive mucosa [Small nose bleeds], Varicose veins and haemorrhoids, Duodenal ulcers, Spastic colitis, Decrease in visual acuity, Headaches, Severe joint pain, Intense muscular pain, Neurological disturbances

After 4 years of exposure, the individual tends to recognize the existence of memory lapses, mood changes become more pronounced, and a variety of simultaneous ailments can appear. In the advanced stages, neurological disorders include epilepsy ?16?, balance disorders ?17?, and a marked increase in cognitive impairment. The palmo-mental reflex - a

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N. A. A. Castelo Branco, M.D., is Head of the Scientific Board, Center for Human Performance, Alverca, Portugal, and is the Principal Investigator of the Vibroacoustic Disease Project. (phone: +351-93-758-4261; fax: +351-21-795-7300; email: ncbranco@oninet.pt).

A. J. F. Martinho Pimenta, M.D., is the Head of the Department of Neurophysiology, Santo António dos Capuchos Hospital, Lisbon, Portugal.

J. M. Reis Ferreira, M.D., is Head Department of Pneumology, Portuguese Air Force Hospital, Lisbon, Portugal (email: reisferreira@hotmail.com).

M. Alves-Pereira, MSc, is a PhD candidate at the Department of Environmental Sciences and Engineering, New University of Lisbon, Caparica, Portugal, and Assistant Coordinator of the Vibroacoustic Disease Project. (mariana.pereira@oninet.pt).

primitive reflex that is frequently present in several pathologies associated with cognitive deterioration – is a common feature in VAD patients [18]. Facial dyskinesia triggered by auditory stimulus has also been identified in LFN-exposed workers [19]. Psychiatric disorders, such as suicidal tendencies and rage-reactions are some of the most tragic consequences of unmonitored LFN exposure [5]. Respiratory disorders appear within the first 4 years of exposure, and can progress into shortness of breath, and, focal pulmonary fibrosis. This is independent of smoking habits [9].

LFN also affects the auditory pathway. One of the complaints that most instigates suspicion of excessive exposure to LFN is “I hear too much”, or “any noise bothers me, television, music, etc”. This is typical in VAD patients [1]. The ensuing behavior is isolation, unlike the behavior of the hearing impaired who do not seek to avoid social gatherings. In the cochlea of LFN-exposed rats, cilia were seen to fuse with the upper tectonic membrane whereas non-exposed rats lost cilia with the normal aging process [11]. Since cilia are fused, it seems natural that any movement they are forced to have will produce discomfort. It is postulated that this may be the reason why VAD patients have these specific auditory complaints.

The need to monitor VAD is most pressing within occupational settings. The appearance of compulsory early disability retirements among LFN-exposed workers due to the definitive and irreversible lesions caused by LFN exposure is an important issue, especially for occupational physicians [5], [20]. It would be useful to have a medical diagnostic test that could reliably and conclusively indicate if the individual was suffering from VAD, and to what degree.

LFN does not only exist in the workplace. Indeed, many leisurely activities now include a great amount of LFN exposure, such as dance clubs, motorized sports, and boom-cars. To work in LFN environments, it is important to select individuals who, despite possible previous exposures to LFN, have not yet developed any VAD signs or symptoms. Again, a medical device that could monitor the progression of LFN-induced lesions would be very useful for this purpose.

This entire problem is aggravated by the lack of recognition that LFN exists and is an agent of disease [21]. While the debate goes on between lobbyists, politicians and legislators, the need for a reliable diagnostic test that would also reflect the degree of progression of the disease is critical. It is crucial to be able to follow the disease so that its lesions do not develop into irreversible conditions that, ultimately, can lead to early disablity retirements, with all the socio-economical sequelae that this entails.

II. Monitoring VAD

A. Through Psychometric and Performance Tests

In 1980, it was discovered that 10% of the aeronautical technicians employed at an aircraft manufacturing, maintenance and repair facility had been diagnosed with late-onset epilepsy; the expected rate for the Portuguese general population is 0.2% [16], [22]. This finding initiated research which led to the definition of VAD. At that time, it was assumed that these technicians’ pathology was exclusively of the neuropsychological domain. Thus, psychological evaluations and psychometric tests were provided for these individuals. Unfortunately, the dispersion of values, low accuracy, and enormous individual variance doomed psychometric tests as a routine tool for VAD [23]. Nevertheless, psychometric tests did reveal cognitive changes in memory and attention [24]. Hence, a computerized test to evaluate worker performance (PACT) was developed [25], but lack of funding did not allow the expansion of this project.

B. Biochemistry

Hematological, biochemical and endocrine studies revealed a very interesting amount of data but useless for a monitoring tool [26]-[30].

C. Through MRI and Neurophysiology

Given the abnormal neurological findings in these patients, brainstem auditory evoked potentials were provided to evaluate possible nerve conduction disturbances [31]. Results were initially difficult to interpret. The problem was tackled mathematically using multivariate analysis, clustering algorithms, of the distribution of action currents. The results were very interesting: delays in nerve conduction were statistically significantly altered in waves III, IV and V [32], [33]. Despite the encouraging advancements, this methodology did not prove to be a useful tool because the technology is expensive and specialists are required. Moreover, despite the mathematical treatment, dispersion values were still quite large. But the results raised suspicions that the brainstem was being compromised.

Initially, magnetic resonance imaging (MRI) of the brain was proposed as a possible method of viewing the brain lesions responsible for the nerve conduction delays. Brain MRI were carried out, and lesions were observed in the subcortical and periventricular white substance, basal ganglia and brainstem [34]-[37]. These features are common to aging processes, as well as to other pathology, and are considered a risk factor for cardio-cerebro-vascular disease. Similarly, cerebral atrophy and dilation of the Virchow-Robin perivascular spaces were also seen in LFN-exposed individuals, but these features are also common to other pathologies. The study of endogenous potentials and brain-mapping confirmed the existence of significant abnormalities in brain potential amplitude and topography, as is usually seen in the elderly and in degenerative processes. A possible VAD-specific correlation was identified between the latency in N2 and the existence of brain lesions [38].

Despite the magnificence of all this neurological information, no consistent, inexpensive and readily available diagnostic tool had yet been identified.

D. Through the Cardiovascular System

In 1987, an autopsy performed on a deceased VAD patient provided outstanding information about this non-specific, and almost silent pathology [8]. The deceased patient exhibited systemic changes of the extra-cellular matrix, with impressive and peculiar thickening of cardiovascular structures. Thickening of all hollow organ walls was identified (even the wall of kidney cysts), and focal fibrosis of the lung was also observed. Two malignant tumors (kidney and brain) were identified. This patient died due to myocardial perforation, as a consequence of a very small infarct and subsequent cardiac tamponade. Studies revealed the presence of 11 small scars dispersed throughout the myocardium indicating that, over the years, 11 silent ischemic events had occurred.

Based on the findings of cardiovascular thickening, the following years were dedicated to the echo-imaging of these structures [39], [40]. Pericardial thickening proved to be the most consistent feature in echocardiograms of VAD patients, although mitral and aortic valve thickening, as well as mitral valve prolapse, were also very frequent findings [4], [41]. Thickened pericardial structures are common in pericarditis which involves an inflammatory process of the tissues. In VAD, despite increased thickness, there is no inflammatory process, nor is there any interference with normal diastolic heart function.

Skepticism surfaced regarding the true anatomical thickeness of the pericardium. Echo-imaging was not a direct reflection of the actual amount of anatomical thickening. With each individual's consent, VAD patients who were submitted to cardiac surgery for other reasons allowed the removal of a fragment of the parietal pericardium for histological and ultrastructural studies. Extraordinary changes of the pericardial structure were observed [2], [6], [7]. Normal pericardial thickness is <0.5 mm. In VAD patients, pericardial thickeness reached 2.3mm [7]. Today, pericardial thickening in the absence of an inflammatory process, and with no diastolic dysfunction, is the hallmark of VAD [42].

Finally, it seemed that a possible diagnostic technique was becoming available. Echocardiography seemed to be the best tool for monitoring VAD. In commercial aircraft pilots [3] and in a civilian population exposed to environmental LFN [4], echocardiography results were consistent: all revealed pericardial thickening in the absence of an inflammatory process and with no diastolic dysfunction. It was the most frequent finding in LFN-exposed individuals, independent of age, and was directly related to the amount of cumulative LFN exposure.

New problems arose when technician subjectivity began to interfere with the consistency of results. All our echocardiography studies had always been performed by the same cardiologists (not technicians) whose specialty was echo-imaging techniques. No standardized method exists for enhancing the pericardial image in order to evaluate its thickness. Thus, echocardiography became a weak parameter for reliably monitoring VAD.

Given the widespread involvement of the cardiovascular system, the carotid arteries as seen through echo-Doppler imaging techniques, became the object of investigation. For the carotid arteries, the acoustic ultrasound window is larger and the vessels are closer to the surface, and thus far easier to evaluate than the heart. Several studies demonstrated that the carotid arteries in these patients were thickened [43]-[45]. Unlike atherosclerotic plaques, here thickening blanketed the entire vessel walls. The results were very promising, but, in Portugal, echo-Doppler technology is relatively expensive, it only exists in major vascular surgery departments, and since no technicians are available, it is usually the vascular disease specialist that conducts echo-imaging evaluations. So this method for diagnosing VAD is not cheap, and requires expensive human resources. Moreover, carotid thickening was not as frequent a finding as cardiac thickening, nor did it reliably reflective the severity of the disease.

E. Through the Respiratory System

During the 1987 autopsy, the observation of lung fibrosis was not immediately associated with LFN exposure. This patient had worked as an aircraft technician, and aircraft run-up tests were part of his job description. Here, the possibility of fumes and dusts is real and could explain the observation in the respiratory tract. However, when these same lesions appeared in small rodents exposed solely to LFN [46], the autopsy findings were questioned. Since then, subsequent respiratory tract studies in rodents exposed to LFN clearly indicates that the respiratory system is a preferential target for LFN [11].

In order to verify that focal lung fibrosis could be a consequence of LFN exposure, high resolution CT-scan of non-smoker, LFN exposed workers, with and without respiratory symptoms was performed. Both groups revealed focal lung fibrosis and air-trapping that was independent of the existence of respiratory complaints. Pulmonary function tests were all within normal values. Curiously, an increased reaction to metacholine was detected [9]. Although about 10% of the general population exhibit an increased sensitivity to metacholine due to allergic propensities, these individuals had been screened for allergic predispositons. Again, and despite the noteworthy results that were obtained, this did not seem to be the best way to monitor LFN-induced lesions.

The respiratory epithelia - surface of the respiratory tract that is open to the airway - of rodents exposed to LFN is dramatically altered [11]. The amount of cilia is reduced but, more remarkably, some cilia appeared sheared, leaving stems of different sizes. Bundles of sheared cilia were found lying upon the epithelial surface. Another unusual aspect was wilted and shaggy cilia that were long but apparently could not remain upright. Brush cells are common in the respiratory epithelia, however their function is unknown. In the LFN-exposed rodents, these brush cells have an extraordinarily peculiar behavior, in that their constituents fuse, much in the same way that cochlear cilia have also fused [11]. Within the cell body of these brush cells, multivesicular bodies have been identified and associated with neuropeptides [47]. The current working hypothesis has been that the respiratory brush cell mediates a neuroendocrine response. This position is

strengthened by the fact that both cilia and brush cells appear to engage in secretion functions, in both controls and LFN-exposed rodents ?11?. Again, despite the wealth of information gathered, no clear method of monitoring VAD in LFN-exposed workers has been achieved.

III. Ongoing Investigation

The clinical manifestations of the neurological lesions in the LFN-exposed workers that have been studied are extraordinary. In a group of 60 workers with an average age of 42 years, 62% (37) exhibited MRI abnormalities that are normally seen in aging processes ?38?. In a group of 40 workers with an average age of 43 years, auditory evoked potentials and brainmapping demonstrate that all had changes associated with cognitive deterioration, as seen in the elderly and in degenerative processes ?38?. In a group of 60 workers with average age 43 years, 30 exhibited the palmo-mental reflex that is frequently present in several pathologies associated with cognitive deterioration ?18?. In a group of 140 workers, average age 42 years, 57% (80) suffered vertigo or dizziness vs. the expected 2% in the general population ?17?. Auditory-induced facial dyskinesia was observed in 4 patients (37-44 years old) ?19?. All EEGs of this study population were within normal values.

This information taken together with that obtained in the respiratory tract of LFN-exposed rodents has now led to question whether the respiratory reflex might be compromised. Ventilation is extremely sensitive to increasing pressures of CO_2 (PCO_2), and less so to decreasing pressures of O_2. Detection of CO_2 changes can occur through peripheral or medullary chemoreceptors. The index $P_{0.1}$ is a measure of the suction developed at the mouth 0.1 seconds after the start of inspiration. This initial respiratory drive originates in the autonomic (or involuntary) pathway of the neural control of the respiratory function. By rebreathing CO_2, normal individuals would present a minimum seven-fold increase in the $P_{0.1}(CO_2)$ index when compared to normal $P_{0.1}$. If the neural control of respiration is compromised, then a less-than seven-fold increase would be expected in the $P_{0.1}(CO_2)$ index ?48?-?50?.

Within this context, a standard test of measuring the amount of ventilation produced by an increase of CO_2 was employed: closed-circuit, or rebreathing technique. This method is normally used to investigate obstructive pathology, which creates local increase of CO_2 and a loss of respiratory drive. Preliminary results indicate that this ventilation test has, indeed, the potential of becoming the reliable, inexpensive and non-invasive diagnostic tool for monitoring VAD. All VAD patients have been presenting abnormal values for the $P_{0.1}(CO_2)/ P_{0.1}$ ratio, or the $P_{0.1}(CO_2)/ P_{IMax}$ ratio (P_{IMax} is the maximal inspiratory pressure). Formal results will be ready for publication in early 2003.

IV. Final Commentary

A very important issue related to VAD and LFN-induced pathology is the difficulty of finding an adequate control population. Who is *not* exposed to LFN? The younger generations are exposed to LFN since their early teenage years, through the variety of leisurely activities that involve very large amounts of LFN. In urban settings, traffic and public transportation are recognized sources of noise in general, and of LFN in particular. False controls, therefore, abound. Some curious cases of false controls have already been described ?5?. One of the most remarkable instances of false controls in LFN-induced pathology is the Vieques heart study ?51?.

The lack of recognition of LFN as agent of disease and the continued erroneous assumption that noise only affects the ear impedes objective and conclusive scientific results. But this status quo situation is tolerated by many and convenient for a few.

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