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ScienceDirect
Environmental Research 107 (2008) 124–131
Environmental Research
www.elsevier.com/locate/envres

# Visual field losses in workers exposed to mercury vapor ☆, ☆☆

Mirella Telles Salgueiro Barboni[a,b,*], Marcelo Fernandes da Costa[a,b], Ana Laura de Araújo Moura[a,b], Cláudia Feitosa-Santana[a,b], Mirella Gualtieri[a,b], Marcos Lago[a,b], Marcília de Araújo Medrado-Faria[c], Luiz Carlos de Lima Silveira[d,e], Dora Fix Ventura[a,b]

[a]*Departamento de Psicologia Experimental, Instituto de Psicologia, Universidade de São Paulo, SP, Brazil*
[b]*Núcleo de Apoio à Pesquisa em Neurociências e Comportamento, Universidade de São Paulo, SP, Brazil*
[c]*Serviço de Saúde Ocupacional do Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, SP, Brazil*
[d]*Departamento de Fisiologia, Centro de Ciências Biológicas, Universidade Federal do Pará, Belém, PA, Brazil*
[e]*Núcleo de Medicina Tropical, Universidade Federal do Pará, Belém, PA, Brazil*

Received 1 February 2007; received in revised form 29 April 2007; accepted 9 July 2007
Available online 23 August 2007

**Abstract**

Visual field losses associated with mercury (Hg) exposure have only been assessed in patients exposed to methylmercury. Here we evaluate the automated visual field in 35 ex-workers (30 males; $44.20 \pm 5.92$ years) occupationaly exposed to mercury vapor and 34 controls (21 males; $43.29 \pm 8.33$ years). Visual fields were analyzed with the Humphrey Field Analyzer II (model 750i) using two tests: the standard automated perimetry (SAP, white-on-white) and the short wavelength automated perimetry (SWAP, blue-on-yellow) at 76 locations within a 27° central visual field. Results were analyzed as the mean of the sensitivities measured at the fovea, and at five successive concentric rings, of increasing eccentricity, within the central field. Compared to controls, visual field sensitivities of the experimental group measured using SAP were lower for the fovea as well as for all five eccentricity rings ($p < 0.05$). Sensitivities were significantly lower in the SWAP test ($p < 0.05$) for four of the five extra-foveal eccentricity rings; they were not significant for the fovea ($p = 0.584$) or for the 15° eccentricity ring ($p = 0.965$). These results suggest a widespread reduction of sensitivity in both visual field tests. Previous reports in the literature describe moderate to severe concentric constriction of the visual field in subjects with methylmercury intoxication measured manually with the Goldman perimeter. The present results amplify concerns regarding potential medical risks of exposure to environmental mercury sources by demonstrating significant and widespread reductions of visual sensitivity using the more reliable automated perimetry.
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*Keywords:* Mercury vapor; Neurotoxicology; Vision; Visual field; Automated perimetry

## 1. Introduction

Mercury intoxication is characterized by lung and renal impairment, and neuromuscular disorders including tremor and weakening of the muscles, as well as neuropsychological changes such as irritability, fatigue, loss of self-confidence, depression, anxiety, delirium, insomnia, apathy, loss of memory, headache, and general pain (Hunter and Russell, 1954).

The nervous system is considered to be a critically vulnerable organ for mercury vapor toxicity in humans (Bast-Pettersen et al., 2005; Chang and Hartmann, 1972a, b;

☆*Financial support*: This study was supported by grants to DFV from the Brazilian Agencies FAPESP (Projeto Temático 02/12733-8), CNPq (523303/95-5), and to DFV and LCLS from CAPES/PROCAD (0019/01-1). It is also supported by the FINEP research grant IBN-Net "Rede Instituto Brasileiro de Neurociência" (01.06.0842-00). MTSB, CFS and MG have FAPESP graduate fellowships, respectively for Master's (05/57897-6) and Doctoral (05/53974-6) and 04/15926-7) work. LCLS and DFV are CNPq Research Fellows.

☆☆We declare that this study was approved by the Ethics Committee of the Institute of Psychology of the University of São Paulo (São Paulo, SP, Brazil) on December 06, 2005, Project #0606.

*Corresponding author. Av. Prof. Mello Moraes, 1721, Bloco A, Sala D9, 05508-900 São Paulo, SP, Brazil.
*E-mail address:* mirellabarboni@usp.br (M.T.S. Barboni).

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doi:10.1016/j.envres.2007.07.004

Chang, 1977; Ellingsen et al., 1993, 2001; Kishi et al., 1993; Urban et al., 1996, 2003). High brain mercury concentrations have been found in humans who died several years after the cessation of exposure to elemental mercury (Hargreaves et al., 1988; Kosta et al., 1975). The lung absorption of mercury vapor is about 80%, and two-thirds of this is immediately transported to other tissues via the blood stream (Nielsen-Kudsk, 1965; Magos and Clarkson, 2006). Mercury penetrates into the nervous tissue through the blood–brain barrier and enters the nerve cells (Chang and Hartmann, 1972b). The neurotoxic effect can be explained by damage caused to the cell membrane structure by mercury ions forming cross-linkages with membrane proteins, and by inhibition of certain associated enzymes. In addition, intracellular mercury can induce apoptosis, which may be an important factor in the pathophysiology of neurodegenerative diseases (Toimela and Tahti, 2004).

Mercury vapor is known to have a toxic effect on the human visual system. The visual impairment is detectable at the cortical level (Ventura et al., 2005) but its origin may lie mostly in the losses seen in mercury intoxication (Ventura et al., 2004). In adult monkeys exposed to mercury vapor by inhalation, autometallographic techniques show that mercury accumulates in the ocular tissues and remains there for a long period of time (Warfvinge and Bruun, 1996). In the retina, mercury accumulates in both glia and neurons, with some differences in accumulation being noted between central and peripheral retinal regions (Warfvinge and Bruun, 1996).

In humans, mercury vapor intoxication leads to impairment of different visual functions that have been demonstrated by psychophysical and electrophysiological methods (Silveira et al., 2003; Ventura et al., 2004). The visual deficits include a decrease of contrast sensitivity in children and adults (Altmann et al., 1998; Silveira et al., 2003; Ventura et al., 2005; Rodrigues et al., 2007), and mild to pronounced color discrimination losses (Cavalleri et al., 1995; Cavalleri and Gobba, 1998; Gobba, 2000; Silveira et al., 2003; Ventura et al., 2005; Feitosa-Santana et al., 2007; Rodrigues et al., 2007) and alterations in subjective color space (Feitosa-Santana et al., 2006).

Previous visual field measurements of patients exposed to methylmercury ingested in food revealed moderate to severe concentric visual field constriction in patients with Minamata disease, and this impairment was significantly correlated with magnetic resonance imaging showing lesions in the calcarine cortex (Korogi et al., 1997). There are likely to be differences between methylmercury and mercury vapor intoxication, since the kinetics and biotransformation of mercury depends on its chemical and physical form (WHO, 2003). Thus, the objective of the present study was to measure the visual field sensitivity by psychophysical perimetry in individuals previously exposed to mercury vapor.

## 2. Materials and methods

### 2.1. Subjects

We evaluated 35 retired workers of fluorescent lamp factories of São Paulo (Brazil) (30 male, mean = 44.2±5.92 years, range from 34 to 56 years), which were sent to us by the Occupational Health Service, School of Medicine, University of São Paulo (Table 1). The subjects had been placed on disability retirement following official diagnosis of mercury intoxication. Their average exposure time to mercury vapor was 10.11±4.74 years and the average number of years away from exposure was 7.53±4.4 years. A control group was comprised of 34 healthy age-matched individuals (21 male, mean = 43.29±8.33 years, range from 30 to 60 years).

Inclusion criteria were that participants had to have Snellen VA 20/25 or better, an absence of ophthalmologic disease or diseases that affect the visual system (i.e. diabetes, multiple sclerosis), and had to be non smokers. Subjects with history of alcoholism, occupational exposure to other toxic substances or with congenital color vision deficiencies were excluded.

All subjects (patients and controls) underwent a complete ophthalmologic examination and an anamnesis.

Informed consent was obtained from all subjects. The procedures complied with the tenets of the Declaration of Helsinki and were approved by the Ethics Committee (Project # 0606) of the Institute of Psychology of the University of São Paulo (Brazil).

### 2.2. Equipment and procedure

There are different methods to perform measurement of visual field sensitivities such as manual kinetic perimetry using a Goldmann perimeter that allows analysis of the entire visual field, and automated static perimetry that provides a reliable, accurate, and reproducible method of visual field testing, but is restricted to 30° or 60°. In the present study, we used the Humphrey Field Analyzer II-model 750i (Humphrey Instruments, San Leandro, California, USA) to measure light sensitivity against a contrast-illuminated background. Two tests were performed in random order for different subjects. One was *standard automated perimetry* (SAP) that utilizes the Swedish Interactive Threshold Algorithm (SITA). We used the Standard central 30-2 strategy. At each visual field location, a 0.43° (4 mm$^2$, viewed at 30 cm; Goldmann III) spot of white light is presented on a 10 cd/m$^2$ white background for 200 ms. This test is usually termed "conventional perimetry" or "white-on-white perimetry". The other test used was *short wavelength automated perimetry* (SWAP), using the Full Threshold central 30-2 strategy, usually termed "blue-on-yellow perimetry". For this test, the stimuli were blue (440 nm) 1.72° (64 mm$^2$ viewed at 30 cm; Goldmann V) spots of light presented for 200 ms on a 100 cd/m$^2$ yellow background. The SWAP protocol preferentially stimulates S-cones by utilizing a blue stimulus presented on a high luminance yellow background to adapt the M and L-cones and to saturate the activity of the rods (Wild, 2001).

All experimental observers were optically corrected for the test distance. The observer's task was to press a button to indicate the presence of the light spot whenever it was detected. Visual field locations of reduced sensitivity relative to controls required brighter stimuli to reach threshold, and had lower decibel (dB) sensitivity values. Similarly, higher dB values represented more sensitive retinal locations (where 1 dB = 0.1 log unit). Sequences of test stimuli were presented randomly throughout the entire visual field, and the sensitivity at each location was determined by the standard Humphrey staircase procedure: the spot intensity was increased in steps of 4 dB until the patient responded with a 'yes' (seen), then it was decreased in steps of 2 dB until the patient responded 'no' (not seen). After two such reversals, the visual threshold was calculated as the average of the four measurements.

Prior to measuring the full array of visual field locations, foveal sensitivity was measured using the Humphrey's 4–2 bracketing strategy with a 30 dB initial stimulus intensity. Once the foveal test was completed, the subject was asked to fixate on the central target and thresholds were

Table 1
Demographic information and mean deviation index of the SAP and SWAP tests for the 35 mercury-intoxicated patients

| ID | Sex | Age (years) | Drafted eye | VA | Exp | Away | Hg | MD SAP | MD SWAP |
|---|---|---|---|---|---|---|---|---|---|
| 1 | M | 37 | OD | 20/20 | 4 | 11 | 1.00 | −3.84 | −3.10 |
| 2 | F | 54 | OD | 20/20 | 12 | 20 | 1.00 | −3.55 | −10.23 |
| 3 | M | 45 | OD | 20/20 | 13 | 2 | 1.00 | −4.46 | −6.70 |
| 4 | M | 50 | OS | 20/20 | 8 | 2 | 1.00 | −2.44 | −9.59 |
| 5 | M | 49 | OD | 20/20 | 7 | 15 | 1.50 | −14.57 | −12.45 |
| 6 | M | 49 | OS | 20/20 | 8 | 8 | 1.00 | −2.24 | −7.08 |
| 7 | M | 43 | OS | 20/25 | 10 | 5 | 1.00 | −1.54 | −3.42 |
| 8 | M | 41 | OD | 20/20 | 9 | 7 | 1.00 | −4.94 | −6.46 |
| 9 | M | 46 | OS | 20/20 | 8 | 6 | 4.30 | −1.33 | −5.48 |
| 10 | M | 37 | OS | 20/25 | 7 | 10 | 1.00 | −4.68 | −8.37 |
| 11 | F | 42 | OS | 20/20 | 11 | 5 | 1.00 | −2.18 | −7.93 |
| 12 | M | 49 | OS | 20/20 | 5 | 11 | 1.00 | −1.71 | −3.81 |
| 13 | M | 48 | OD | 20/20 | 12 | 3 | 1.00 | −0.61 | −2.96 |
| 14 | M | 37 | OS | 20/20 | 8 | 5 | 1.00 | 0.23 | −2.11 |
| 15 | M | 47 | OD | 20/20 | 24 | 2 | 1.00 | −4.03 | −13.33 |
| 16 | M | 35 | OS | 20/20 | 7 | 8 | 1.00 | −9.37 | −11.86 |
| 17 | M | 38 | OS | 20/25 | 14 | 2 | 1.40 | −1.33 | −5.35 |
| 18 | M | 36 | OS | 20/20 | 6 | 7 | 1.00 | −7.34 | −4.11 |
| 19 | M | 52 | OD | 20/25 | 9 | 9 | 1.00 | −2.64 | −4.86 |
| 20 | M | 44 | OD | 20/20 | 25 | 3 | 1.00 | −3.53 | −5.42 |
| 21 | M | 40 | OD | 20/20 | 10 | 5 | 1.00 | −0.90 | −4.11 |
| 22 | M | 56 | OS | 20/20 | 11 | 10 | 1.30 | −1.23 | −2.76 |
| 23 | M | 45 | OS | 20/20 | 12 | 16 | 1.00 | −1.75 | 0.52 |
| 24 | M | 48 | OS | 20/20 | 7 | 9 | 1.30 | −0.93 | 1.37 |
| 25 | M | 34 | OS | 20/20 | 9 | 6 | 1.80 | −2.53 | −2.37 |
| 26 | M | 45 | OD | 20/20 | 12 | 9 | 1.00 | −1.86 | 2.12 |
| 27 | F | 38 | OD | 20/20 | 12 | 5 | 2.10 | −2.49 | −9.35 |
| 28 | F | 45 | OS | 20/20 | 1 | 5 | 1.00 | −3.79 | −14.61 |
| 29 | M | 35 | OS | 20/25 | 15 | 5 | 1.00 | −4.01 | −12.76 |
| 30 | M | 47 | OS | 20/20 | 17 | 4 | 1.00 | −6.12 | −0.98 |
| 31 | M | 47 | OD | 20/25 | 10 | 15 | 4.50 | −3.14 | −7.21 |
| 32 | F | 47 | OD | 20/20 | 10 | 6 | 1.00 | −3.54 | −1.14 |
| 33 | M | 51 | OS | 20/20 | 8 | 7 | 1.00 | −3.44 | −8.49 |
| 34 | M | 39 | OD | 20/20 | 7 | 13 | 3.30 | −1.95 | −2.59 |
| 35 | M | 51 | OD | 20/20 | 8 | 9 | 1.00 | −1.89 | −2.09 |
| Mean | | 44.20 | | | 10.11 | 7.53 | 2.39 | −3.30 | −5.69 |
| (SD) | | 5.92 | | | 4.74 | 4.40 | 1.30 | 2.75 | 4.28 |
| Min | | 34.00 | | | 1.00 | 2.00 | 1.00 | −14.57 | −14.61 |
| Max | | 56.00 | | | 25.00 | 20.00 | 4.50 | 0.23 | 0.52 |

ID = subject identification; VA = visual acuity; OD = right eye (oculum destrum); OS = left eye (oculum sinistrum); Exp. = exposure duration; Away = time away from exposure to the mercury source; Hg = mean urinary concentration of Hg-μg/g creatinine-at the time of visual field testing; MD SAP = mean deviation for standard automated perimetry; MD SWAP = mean deviation for short wavelength automated perimetry.

measured at different locations in the visual field by the presentation of small spots of light of different intensity. SAP involves determining the minimum luminance necessary for the patient to detect the presentation of a static white light stimulus of constant size presented at various locations of the visual field. In automated perimetry, the test algorithms make use of an empirical model of the "hill of vision" of normal observers. The significance of overall deviations or patterns of deviations across the visual field (the perimetry global indices) is quantified with respect to the mean and variance of the visual field data of normal, age-matched observers.

The SITA program used in the SAP test reduces test time by approximately 50% when compared with the full threshold program used in SWAP test, because the number of stimuli presented is 29% smaller in normal fields (Bengtsson et al., 1997). It is a more reliable psychophysical paradigm to measure localized threshold. Reliability and efficiency of the SITA algorithm is enhanced by (1) use of information about surrounding points, (2) use of information about threshold values in age-matched controls, (3) reacting to changes in the pacing of the test, (4) elimination of retest trials for the 10 points used to calculate short-term fluctuation in the full threshold algorithm used in SWAP, (5) an improved method of evaluating false positive and false negative reliability parameters, and (5) use of a maximum likelihood procedre for 18–20 estimatates of threshold (Bengtsson et al., 1997). The SITA program was used only in SAP, and the traditional full threshold strategy was performed in SWAP (Johnson et al., 1992).

The results were expressed as mean deviation (MD) which is a location-weighted mean of the values in the total deviation plot. It is essentially a distilled value that represents the average height of the entire "hill of vision". Negative values represent depressed sensitivity (sensitivity loss). MD is relatively insensitive to localized defects and is strongly affected by generalized trends. The results were also expressed in pattern standard deviation (PSD) which represents the unevenness of the "hill of vision" surface. PSD is calculated by taking a location-weighted standard deviation of all sensitivity values. PSD is insensitive to the overall average height and is strongly affected by localized defects.

Both eyes of the patients and the controls were tested monocularly, with the right eye and left eye measures done in random order. Each test

was performed in one or two sessions interleaved with rest periods in order to avoid fatigue effects (Hudson et al., 1994). The tests were performed in an otherwise dark room and fixation was monitored by the experimenter throughout the test. If fixation deviations reached 20%, or if false-positive or false-negative errors reached 33%, the session was terminated and the test was repeated on a different day.

The mercury intoxication level in the patients was assayed by measuring Hg in urinary creatinine. Mercury level, in μg Hg/g urinary creatinine, was measured using atomic absorption spectrophotometry that involves reduction, aeration, and reading of mercury vapor absorption at 253.7 nm in a quartz cell (Hatch and Ott, 1968; Wittmann, 1981). For the purposes of the statistical analyses, data from all subjects with urine Hg concentration $<1$ μg/g of creatinine were treated as if their levels were equal to 1 μg Hg/g urinary creatinine.

### 2.3. Analysis

The results were analyzed with the program Stastistica 6.0 (StatSoft, Inc., USA). For each subject, eight measures were calculated: the two global indices MD and PSD, foveal threshold, and the mean of the sensitivities measured at each of the five concentric eccentricity rings (Fig. 1). Statistical analysis was performed on the data from only one eye of each subject, and was randomly chosen. We used the nonparametric Mann–Whitney Test to compare the sensitivity data bewteen groups. For the correlation analyses, we used the Spearman $R$ correlation coefficient. In all analyses, $p$-values $<0.05$ were considered to be statistically significant.

## 3. Results

The mean mercury level measured in the patients was $41.15\pm1.72$ μg Hg/g urinary creatinine for as long as 1 year after exposure, and $2.39\pm1.3$ μg Hg/g urinary creatinine (normal levels) at the time of examination, which was performed 7.53 ($\pm4.4$) years following exposure.

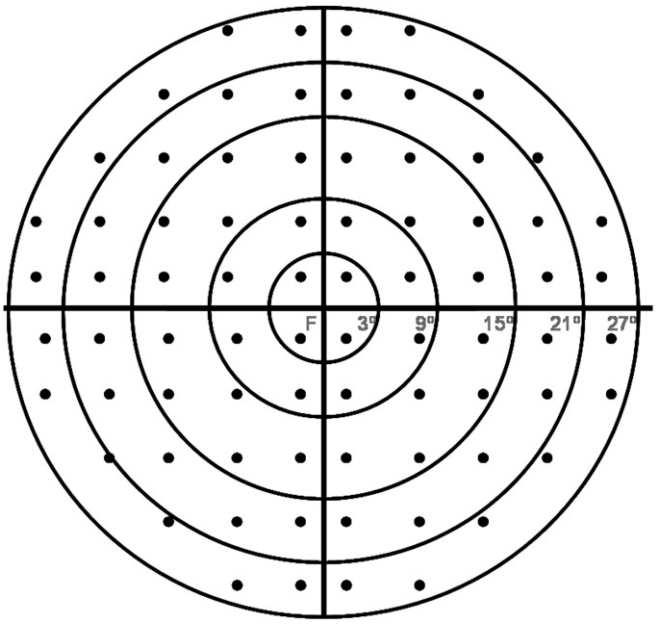


Fig. 1. Diagram showing the visual field position of the six areas that were analyzed. Results were expressed as the mean of the sensitivities measured for each point inside a given ring. The foveal threshold is represented by the central position, and concentric rings indicate the test loci at increasing eccentricities.

The Mann–Whitney test shows no statistical difference for any visual field parameters between the patients with VA 20/20 and VA 20/25 (SAP $p>0.255$ and SWAP $p>0.314$), implying that any differences in visual field measures were not due to acuity differences.

We found no correlation of visual field sensitivity, expressed by the MD with any of the following measures: exposure time (SAP $p=0.626$ and SWAP $p=0.841$), time away from exposure (SAP $p=0.649$ and SWAP $p=0.371$), urinary Hg concentration at the time of exposure or up to 1 year after exposure (SAP $p=0.702$ and SWAP $p=0.644$), or with urinary Hg concentration at the time of the test (SAP $p=0.259$ and SWAP $p=0.967$). We also found no correlation between the average sensitivity measured for each eccentricity ring and any of the above parameters.

The global indices for all patients are summarized in Table 1, along with patient's demographic and acuity data. Table 2 shows that, compared to controls, we found a significant reduction in both tests for MD ($p<0.001$) and PSD ($p<0.001$). Both groups showed sensitivity reductions compared to the standard Humphrey norms, but the sensitivity reduction found in our experimental group is significantly greater than the reduction found in the control group.

Table 3 shows that, for the SAP, we found significant sensitivity reduction for the experimental group relative to the control group at all examined regions: foveal threshold, $p=0.009$; each of the five successive concentric rings, $p<0.001$. This was also true for the SWAP ($p<0.001$), except for the foveal threshold ($p=0.277$) and for the 15° ring ($p=0.965$) (Fig. 2).

We found no statistical differences between genders (male vs. female for controls, $p>0.061$; male vs. female for patients, $p>0.371$), or a dependence on age. Patients and controls were binned into three age groups: 30–40, 41–50, 51–60 years. For both, the patients and controls, no

Table 2
Global indices results of visual field examinations of patients ($n=35$) and controls ($n=34$) using the Humphrey Central 30–2 SITA-Standard white-on-white test (SAP) and Central 30-2 Full Threshold blue-on-yellow test (SWAP)

| | Patients | Controls | $p$-Value |
|---|---|---|---|
| *SAP* (*white-on-white*) | | | |
| MD | $-3.30\pm2.75$ | $-0.70\pm1.24$ | $<0.001$ |
| PSD | $3.07\pm2.00$ | $1.86\pm0.47$ | $<0.001$ |
| *SWAP* (*blue-on-yellow*) | | | |
| MD | $-5.69\pm4.28$ | $-1.60\pm1.73$ | $<0.001$ |
| PSD | $3.85\pm1.16$ | $2.68\pm0.64$ | $<0.001$ |

MD = mean deviation; PSD = pattern standard deviation. Data are given as mean $\pm$ SD in dB. $p$-Values for comparisons were calculated with the nonparametric Mann–Whitney test.

Table 3
Mean of the sensitivities measured in the fovea and at each of five concentric eccentricity rings

| | Patients | Controls | *p*-Value |
|---|---|---|---|
| *SAP* (*white-on-white*) | | | |
| *F* | 34.89±2.15 | 36.24±1.63 | = 0.009 |
| 3° | 30.97±1.80 | 32.84±1.29 | <0.001 |
| 9° | 29.70±1.89 | 31.88±1.27 | <0.001 |
| 15° | 26.28±2.77 | 29.03±1.53 | <0.001 |
| 21° | 25.58±3.84 | 28.89±1.57 | <0.001 |
| 27° | 23.13±4.62 | 27.09±2.11 | <0.001 |
| *SWAP* (*blue-on-yellow*) | | | |
| *F* | 24.23±3.47 | 23.15±3.79 | = 0.277* |
| 3° | 23.40±3.47 | 26.35±2.04 | <0.001 |
| 9° | 21.70±4.14 | 25.18±2.28 | <0.001 |
| 15° | 18.06±4.72 | 22.11±2.17 | = 0.965* |
| 21° | 15.92±5.17 | 20.96±2.52 | <0.001 |
| 27° | 13.59±5.10 | 18.73±3.58 | <0.001 |

*F*: foveal threshold; 3°, 9°, 15°, 21°, 27°: eccentricity rings. Data are given as mean±SD in dB. *p*-Values for comparisons were calculated with the nonparametric Mann–Whitney test. *Note that for the SWAP test, foveal sensitivity and mean sensitivities from the 15° ring were not statistically different from controls.

significant differences in any of the measures were found (*minimum p*-value was 0.073).

## 4. Discussion

We measured visual sensitivity at 76 locations in the central 27° of the visual field in a group of retired workers that were exposed to mercury vapor in their working environment (fluorescent lamp factories). These workers had been previously diagnosed, their working conditions and general pathological symptoms described (Medrado-Faria, 2003; Zavariz and Glina, 1992), and several aspects of their neuropsychological conditions and visual functions quantified (Ventura et al., 2004, 2005; Feitosa-Santana et al., 2006, 2007; Zachi et al., 2007). The effects of mercury intoxication were severe enough that these workers had been placed on disability retirement.

To our knowledge, the present study is the first to document visual field impairment caused by mercury vapor intoxication using automated perimetry. We showed that visual sensitivity is reduced in subjects exposed to mercury vapor, both in the fovea and peripheral regions of the visual field.

Previous studies have shown that methylmercury intoxication via ingestion decreases the sensitivity in the periphery of the visual field—so-called "concentric visual field constriction" (Hunter et al., 1940; Hunter and Russell, 1954; Korogi et al., 1997; Sabelaish and Hilmi, 1976). Results of recent nuclear magnetic resonance imaging suggests that the visual field impairment due to mercury intoxication is well correlated with the damage to the anterior portion of the calcarine cortex at the junction of the calcarine and parieto-occipital fissures where the peripheral visual field is represented (Korogi et al., 1994, 1997, 1998). Concentric visual field constriction is found in 100% of cases of Minamata disease (Chang, 1977; Harada, 1995) and has been explained by lesions in the calcarine cortex (Korogi et al., 1997), in agreement with histological findings in monkeys exposed to methylmercury and mercuric chloride (Charleston et al., 1995).

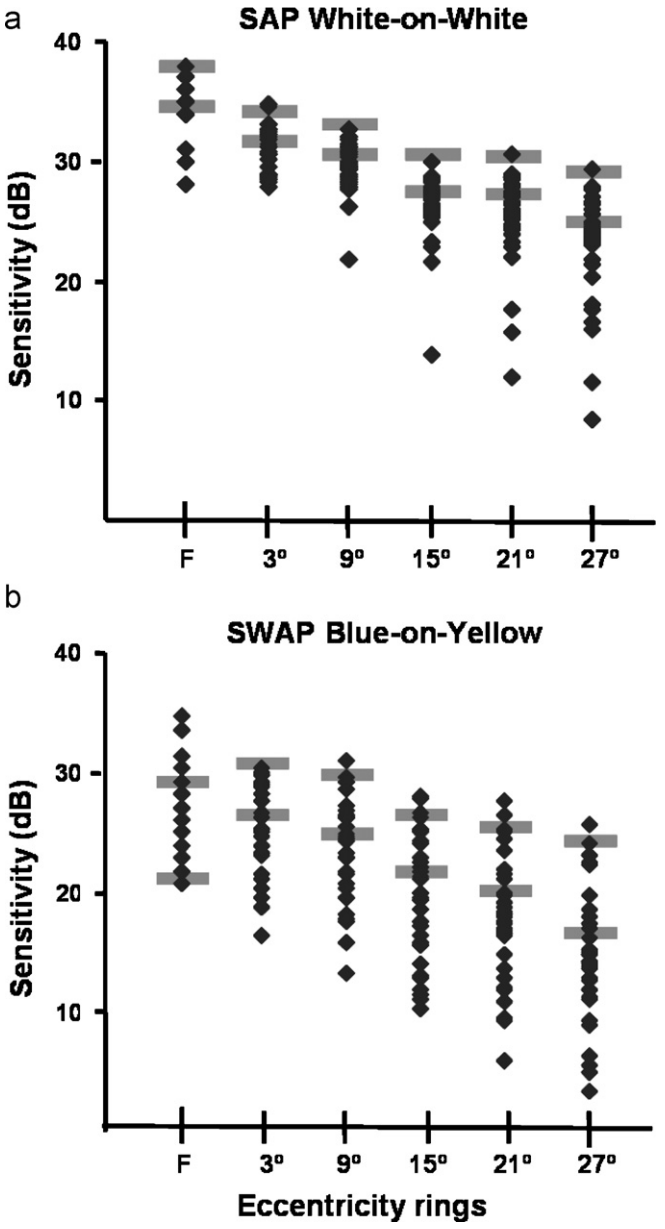


Fig. 2. Visual field results. Mean sensitivity at the fovea and for the locations within five concentric eccentricity rings, from 3 to 27 degrees of visual angle. Normative data are shown by upper and lower limits (gray bars) and the data from the eyes of 35 patients are plotted individually as filled diamonds. (A) SAP we found significant sensitivity reduction for the experimental group relative to the control group at all examined regions: foveal threshold, $p = 0.009$; each of the five successive concentric rings $p < 0.001$. (B) SWAP we found significant sensitivity reduction for the experimental group relative to the control group at all examined regions ($p < 0.001$), except for the foveal threshold ($p = 0.277$) and the 15° ring ($p = 0.965$).

In the early 1970s, there was an outbreak of organo-mercury poisoning in Iraqi farmers who consumed treated

grain. The visual field changes in most of the Iraqi patients examined also had the shape of concentric constriction at all quadrants, and no improvement was found on follow-up examination (Sabelaish and Hilmi, 1976).

Mercury is trapped within the retinal capillary walls and its retention is stable throughout a long period of time (Warfvinge and Bruun, 1996). It quickly penetrates into the nervous tissue through the blood–brain barrier, crosses the neuronal membrane and, as the result of digestion of damaged mercury containing organelles, is sequestered into lysosome dense bodies (Danscher and Schroder, 1979; Graeme and Pollack, 1998). Exposure to mercury vapor has been shown to produce mercury deposits in primate retinas (Warfvinge and Bruun, 1996; Warfvinge and Bruun, 2000). In these studies, the eyes of monkeys exposed to mercury vapor had a high amount of metal found in the optic disc, retinal pigment epithelium, capillary walls, and neural retina. Mercury does not accumulate evenly throughout the retinal layers. For instance, the ganglion cell layer showed mercury deposits in moderate amounts. A detailed topographical analysis showed mercury deposits in the central and mid-peripheral parts of the retina, but not in the peripheral retina (Warfvinge and Bruun, 1996, 2000).

Our results are in agreement with other measurements made in the same subjects (Ventura et al., 2004, 2005; Feitosa-Santana et al., 2007), and with persistent effects on neurobehavioral function for several years after the mercury vapor exposure (Kishi et al., 1993; Zachi et al., 2007). Our previous psychophysical and electrophysiological studies of the central vision in this group of patients showed a moderate to severe impairment of several visual functions. They exhibited psychophysical losses of achromatic contrast sensitivity, chromatic contrast sensitivity, and color discrimination, as well as losses in contrast sensitivity measured by visual evoked potential (Ventura et al., 2004, 2005; Feitosa-Santana et al., 2007). In addition, their full field electroretinograms were altered and their multifocal electroretinograms have decreased amplitudes revealing a loss of the retinal response in the fovea and within the 25 central degrees (Ventura et al., 2004).

In SAP or white-on-white perimetry, we found a reduction in visual sensitivity at all eccentricities from the fovea out to 27° in the periphery. These results are consistent with the decrease of central retinal response found in the multifocal electroretinogram evaluation, and with the losses in functions mediated by central vision such as color discrimination and spatial contrast sensitivity (Ventura et al., 2004, 2005).

The SWAP or blue-on-yellow perimetry has been used for evaluation of different neuro-ophthalmologic disorders (Keltner and Johnson, 1995). It was originaly designed to evaluate the retinal damage in glaucoma since this protocol is designed to target visual processing in the inner retina (Sample, 2000; Polo et al., 2001; Wild, 2001). In the inner retina, some ganglion cells depolarize in response to blue light (which preferentially activates the shortwavelength-sensitive cones) and hyperpolarize in response to yellow light (which activates equally the long and middle wavelength-sensitive cones). These cells are classified as $+S-(M+L)$ (Dacey and Lee, 1994; Lee et al., 1989; Silveira et al., 1999).

Our results from the blue-on-yellow analysis measured in the SWAP protocol revealed that, except for the fovea and for the 15° ring, there were losses in the mercury-exposed group compared with control group at all eccentricities measured. The fact that the foveal blue-on-yellow sensitivity of mercury-exposed group was similar to that of the control group is not surprising given the lack of short-wavelengh cones within the central 3–4° (Curcio et al., 1991; Roorda and Williams, 1999; Calkins, 2001). With respect to the lack of difference between controls and mercury exposed patients in the SWAP protocol, several authors have shown that the blue–yellow mechanism is more robust than the red–green as one moves from the fovea to the periphery (Mullen and Kingdom, 2002) and perhaps this lack of effect suggests that it is less affected at the periphery.

Electroencephalographic changes have been observed in people with chronic exposure to mercury vapor (Urban et al., 2003). In the primary visual cortex (V1), electrophysiological measurement of luminance contrast sensitivities using the visual evoked potential showed that there is impairment in the response to all spatial frequencies as a result of mercury intoxication (Ventura et al., 2005). Similarly, psychophysical measurement of luminance and chromatic contrast sensitivity, as well color vision, show diffuse losses, leading to the conclusion that there is a generalized impairment in the visual pathways as a result of mercury intoxication (Ventura et al., 2005).

In addition, the impairment of function in the periphery, mid-periphery, and central retina found by full field and multifocal electrorretinography could explain reductions in sensitivity found throughout the visual field by SAP evaluation (Ventura et al., 2004).

To our knowledge, the present study constitutes the first assessment of visual field in subjects exposed to mercury vapor. We find that significant losses of sensitivity in both the central and peripheral parts of the visual field persist in patients even after more than an average of 7 years following cessation of exposure. This visual impairment may have a cortical origin, as demonstrated in studies of methylmercury intoxication, but there is also a significant retinal involvement in these losses, since the same patients had demonstrable losses of retinal function in a previous study (Ventura et al., 2004). Previous reports in the literature describe moderate to severe concentric constriction of the visual field in subjects with methylmercury intoxication measured manually with the Goldman perimeter. The present results amplify concerns regarding potential medical risks of exposure to environmental mercury sources by demonstrating significant and widespread reductions of visual sensitivity using the more reliable automated perimetry.

## Acknowledgment

We are grateful to Russell D. Hamer for assistance in editing the manuscript.

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