Neuropsychological Impairment From Acute Low-Level Exposure to Carbon Monoxide

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Objective: To investigate the effects of acute low-level exposure to carbon monoxide on higher cognitive functions in healthy humans.

Design: An empirical study of the effects of low-level exposure to carbon monoxide on higher cognitive functions in young healthy volunteers and a matched non-exposed control group.

Setting: A dormitory at the Hebrew University campus in Jerusalem, Israel.

Participants: Forty-five student volunteers who were exposed to carbon monoxide from residential kerosene stoves for 1.5 to 2.5 hours (air carbon monoxide concentrations of 17-100 ppm; mean ± SD, 61 ± 24 ppm) served as the experimental group and 47 nonexposed students served as the control group.

Main Outcome Measures: A battery of neuropsychological tests was administered to each participant including digit span, the revised Wechsler Memory Scale for verbal and figural memory, Trail-Making Test parts A and B, digit symbol, block design, and the Rey Auditory Verbal Learning Test.

Results: Venous blood carboxyhemoglobin (HbCO) levels in participants of the study group ranged from 0.01 to 0.11 (mean ± SD, 0.04 ± 0.03) and correlated with air carbon monoxide concentrations (r = 0.39; P = .01). The experimental group scored significantly lower than controls on the following tests: digit span forward (P = .02), short-term (P = .008) and long-term semantic memory (P = .008), digit symbol (P = .004), block design (P = .009), recall of figural memory (P = .02), and Trail-Making part A (P = .04). No significant differences were found between the experimental and control groups in other tests.

Conclusions: The lower scores on neuropsychological tests indicate dysfunctions in memory, new learning ability, attention and concentration, tracking skills, visuomotor skills, abstract thinking, and visuospatial planning and processing. These dysfunctions correspond with previous reports of carbon monoxide neurotoxic effects in patients with moderate carbon monoxide poisoning. Low-level exposure to carbon monoxide results in impairment of higher cognitive functions. Neuropsychological testing appears to be sensitive in the detection of subtle neurologic dysfunctions resulting from carbon monoxide poisoning.

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Carbon monoxide poisoning results primarily in cardiac and neurologic damage. The severity of carbon monoxide toxicity ranges from subclinical or occult poisoning to severe morbidity and death. The effect of low-level exposure to carbon monoxide on the heart is well documented. In patients with coronary heart disease, inhalation of slightly elevated concentrations of carbon monoxide in air produces blood carboxyhemoglobin (HbCO) levels of 0.02 to 0.04 and causes coronary ischemia. Carboxyhemoglobin levels of 0.06 have been reported to precipitate cardiac arrhythmias.

The neurologic manifestations that result from exposure to carbon monoxide are diverse. Early symptoms of carbon monoxide neurotoxicity consist of headache and fatigue (HbCO levels, 0.1-0.2), while more advanced symptoms consist of dizziness and syncope (HbCO levels, 0.2-0.3). Further elevations of HbCO levels in the blood are associated with lethargy, coma, seizures, and death.

Signs of carbon monoxide neurotoxicity may occur at low levels of exposure as well. The symptoms may be subtle, nonspecific, and more difficult to detect in a bedside neurologic examination. Messier and Myers constructed a neuropsychological screening battery (CONSB) to improve the neurological assessment of carbon monoxide neurotoxicity. The selection of test subsets was based on previous reports indicating that carbon monoxide poi-
SUBJECTS AND METHODS

The study was approved by the Human Investigation Committee at the Hadassah Medical Center, Jerusalem, Israel, and all participants signed an informed consent form.

SUBJECTS

All participants who volunteered for the study were young and healthy students at the Hebrew University of Jerusalem. There were 45 subjects in the study group and 47 in the control group.

The study group and the control group were matched for age (mean age, 21.8 and 22.2 years, respectively) and sex (12 men and 33 women, and 17 men and 30 women, respectively). Students in both groups studied a wide range of disciplines at the university, including medicine, science, nursing, education, law, psychology, international relations, and social work. The CONSB was administered in Hebrew. Nearly 70% of the participants in both groups were native Hebrew speakers, and all participants were sufficiently fluent in Hebrew. Six participants (13%) in the study group and 8 (17%) of the controls were smokers.

PROCEDURES

Subjects in the study group were exposed to high levels of carbon monoxide from kerosene stoves provided by the dormitory for heating during the winter. The stoves were old and infrequently used by most students. The CONSB was administered to participants in the study group in their rooms, where the kerosene heaters were functioning 1.5 to 2.5 hours before the administration of the test and during the test. The CONSB was administered to the control group participants in a similar environment in their rooms without kerosene heaters.

A modified CONSB was administered to participants in both groups and consisted of the following tests: (1) the revised Wechsler Memory Scale for adults, which assesses short-term and long-term semantic and figural memory; (2) digit symbol, which assesses visuospatial organization and constructional skills; (3) digit span forward and backward, which assess immediate auditory memory, attention, and concentration; (4) Trail-Making Test parts A and B, which assess spatial planning and psychomotor abilities; and (5) the Rey Auditory Verbal Learning Test, which assesses verbal memory and learning ability.

The tests were administered by 2 of us (V.G.-K. and A.W.), who were trained in the administration and evaluation of the test. During the administration of the CONSB, concentrations of carbon monoxide in the air were measured by portable carbon monoxide detectors (Compur Dosidox, Bayer Diagnostics, Munich, Germany). The level of carbon monoxide emission by the stoves was not known before the study. Venous blood samples were drawn from all subjects in the study group immediately after the completion of the CONSB. Blood HbCO levels were measured in duplicate by the spectrophotometric method (Cooximeter 482, Instrumentation Laboratory, Lexington, Mass). The variability between duplicates was less than 5%.

STATISTICAL ANALYSIS

The Pearson product moment correlation test was used for linear regression, and the F test was used for the multivariate analysis of variance in a 2 × 14 design. The Wilcoxon rank sum test was used to compare the CONSB subtest scores of the 2 groups. For all statistical values, a P value of less than .05 was considered significant.

RESULTS

In the study group, carbon monoxide concentrations in room air ranged from 17 to 100 ppm (mean, 61 ppm; SD, 24 ppm). Venous blood HbCO levels ranged from 0.01 to 0.11 (mean, 0.04; SD, 0.03). Twenty subjects had HbCO levels higher than 0.04.

There was a significant correlation between carbon monoxide air concentrations and HbCO levels (r = 0.39; P = .01) (Figure).

The mean performance scores on the subtests for the 2 groups are presented in the Table. The subjects exposed to carbon monoxide scored significantly lower on 7 subtests than participants in the control group. Subjects exposed to carbon monoxide had slightly lower scores on 4 other subtests (Trail-Making Test part B, P = .08; short-term figural memory, P = .17; memory after learning, P = .43; digit span backward, P = .45) and slightly higher scores on 3 subtests (immediate memory, P = .29; recall, P = .34; identification, P = .62), but these differences were not statistically significant.

COMMENT

The neurotoxic effect of moderate and severe carbon monoxide poisoning is well established. However, the extent of neuropsychological damage from milder forms of exposure to carbon monoxide is controversial. Some of the difficulty with defining the degree of

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neurotoxic damage caused by mild exposure to carbon monoxide stems from the fact that symptoms may be occult and nonspecific. In addition, changes in cognition and mental status may be subtle and therefore not easily detected in a bedside neurologic examination. For this reason, Messier and Myers constructed the CONSB to improve the neurologic assessment of patients with carbon monoxide poisoning. The CONSB includes 6 subtests that evaluate higher cognitive functions including memory, visuomotor coordination, visuospatial planning and processing, temporospatial orientation, and constructional skills. Acute carbon monoxide poisoning was reported to be linked to a significant decline in cognitive functions compared with a control group.

In the present study, a modified CONSB was administered to young healthy adults who were exposed to low levels of carbon monoxide. The battery was designed to evaluate the magnitude and severity of the neuropsychological damage from neurotoxic exposure. Tests were chosen on the basis of their sensitivity to higher cognitive functions. The battery was designed to evaluate short-term and long-term semantic and figural memory, immediate auditory memory, attention and concentration, visuomotor coordination, visuospatial organization, constructional skills, spatial planning, and psychomotor abilities.

Exposure was confirmed with individual measurements of carbon monoxide in the air and HbCO levels in the blood. These 2 parameters were significantly correlated with each other.

Low-level exposure to carbon monoxide has been linked to impairment of various neurologic functions. Carboxyhemoglobin levels of 0.03 to 0.05 were associated with a decrease in visual threshold. Exposure to carbon monoxide resulting in similar HbCO levels have caused an impairment of driving skills and auditory duration discrimination. Other researchers have reported a deterioration of choice discrimination with regard to colors and letters at an HbCO level of less than 0.05. In addition, they noted parallel changes in cognitive skills, such as the ability to perform mental arithmetic, underline plural nouns, and cross "s." A deterioration of visual vigilance was observed at an average HbCO level of 0.07, and a decrease in reaction times was reported at a level of 0.05.

The present study indicates that cognitive impairment resulting from low-level exposure to carbon monoxide may be more extensive than previously reported and may involve memory, visuomotor coordination, visuospatial functioning, construction skills, temporospatial orientation, and attention and concentration.

In our study, the high concentrations of carbon monoxide were produced by old kerosene stoves in small rooms with poor ventilation. However, even modern kerosene heaters were found to cause significant elevations in levels of HbCO in residents exposed to such heaters. Tests carried out by the US National Bureau of Standards have revealed that kerosene heaters in small rooms with poor ventilation emit air carbon monoxide concentrations of 46 to 98 ppm, similar to the carbon monoxide levels reported in our study. Thus, our finding that the emission of carbon monoxide by kerosene stoves is associated with impairment of higher cognitive functions may be relevant to other individuals who use kerosene heaters.

Naturally, generalizations from our findings should be considered with caution, but it would seem that an evaluation of the cognitive functions of individuals who have been exposed to low levels of carbon monoxide is certainly warranted.
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REFERENCES


