Continuing Decline of Memory Skills with Significant Recovery of Intellectual Function Following Severe Carbon Monoxide Exposure: Clinical, Psychometric, and Neuroimaging Findings

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Extensive clinical, psychometric, and neuroimaging data are presented and interpreted with regard to a 35-year-old, White male college graduate who was exposed to severe carbon monoxide (CO) poisoning. The patient was comatose for 21 days following the exposure. Several other people, who were in the same room as the patient, died due to the toxic effects of the CO. The patient was employed premorbidly as a systems level lead computer programmer. The patient received medical and neuropsychological follow-up for 3 years post-CO exposure. Neuropsychological evaluations revealed a gradual, but incomplete recovery of general intellectual function. The patient continued to exhibit severe memory deficits with some evidence for small additional memory decline over time. Characteristic and permanent vestibular and gait disturbances were also noted, along with a variety of neuropsychological deficits that improved over time with the exception of memory function. The patient also experienced significant affective and personality changes. Neuroimaging studies reveal a generalized cortical atrophy as shown by significantly enlarged ventricles and a ventricle-to-brain ratio that exceeded 4 standard deviations above the norm. The observed atrophic changes are consistent with CO-induced anoxic

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Carbon monoxide (CO) poisoning is the most common cause of poisoning death and morbidity in the United States (Fawcett et al., 1992; Hartman, 1995). It is estimated that there are as many as 40,000 emergency department visits across the United States per year and 6,000 deaths due to CO poisoning (Cobb & Etzel, 1991; Hampson, 1997). CO is a colorless, odorless, and tasteless gas that is produced from incomplete combustion of organic matter. CO combines with hemoglobin to form carboxyhemoglobin (COHb), which decreases the oxygen carrying capacity of the hemoglobin. Hemoglobin, the major oxygen transport system of the body, has an affinity for CO 200 to 300 times greater than its affinity for oxygen, thus resulting in significant reductions in the concentration of oxygen to the tissues (Corburn & Mayers, 1971). When CO binds to hemoglobin there is a leftward shift of the oxyhemoglobin dissociation curve, which inhibits release of oxygen until very low tissue partial pressures of oxygen are reached (Doblar, Santiago, & Edleman, 1977) resulting in decreased tissue oxygenation. Other mechanisms by which CO poisoning adversely affects mammalian tissues include: (a) binding of CO to various intracellular proteins including P-450 and myoglobin (Corburn & Mayers, 1971; Piantadosi, 1987; Piantadosi, Sylvia, Saltzman, & Jobsis-Vander Vliet, 1985); (b) neuroexcitotoxicity due to massive release of excitatory neurotransmitters, such as glutamate, due to brain anoxia (Jarrard & Meldrun, 1993); (c) lipid peroxidation which leads to neutrophil activation (i.e., ischemia/reperfusion injury; Thom, 1990); (d) endothelial deposition of peroxynitrate which damages the endothelium (Thom, 1993); and (e) apoptosis (i.e., programed cell death; Piantadosi, Schmechel, & Zhang, 1995).

Patients with acute CO poisoning may exhibit nonspecific symptom(s) and the association of specific symptoms with known COHb levels is controversial. Some reports note that CO concentrations of 10% or less may produce mild CNS symptoms, 20% produce throbbing headaches, 30% may cause confusion, vomiting, and impaired cognition, 50% results in unconsciousness, and by 60% CO seizures, coma, and death are common. Other studies show that COHb levels do not correlate with clinical symptoms or with neuropsychological outcome (Burney, Wu, & Nemiroff, 1982; Hopkins, Weaver, Larson-Lohr, & Howe, 1995; Sokal & Kralkowska, 1985).

CO poisoning has been shown to produce delayed encephalopathy, primarily seen as demyelination, degeneration of the periventricular white matter, and necrosis of the globus pallidus (Chang, Han, Kim, Wie, & Han, 1992) that may be conspicuous on MRI but not viewed on CT (Hopkins et al., 1995; Minura, Mitomo, Kawai, & Harada, 1985). Structural abnormalities that occur due to CO poisoning include lesions of the globus pallidus and substantia nigra (Fife, Salle, Gray, & Piantadosi, 1980; Minura et al., 1985; Plum, Posner, & Hain, 1962; Pracyk, Stolp, Fife, Bray, & Piantadosi, 1995), cortical degeneration (Plum et al., 1962), cerebellar lesions (Plum et al., 1962), and diffuse white matter lesions (Minura et al., 1985). Diffuse grey matter lesions, cerebral edema and damage to the hippocampus have also been reported (Hopkins, Weaver, & Kesner, 1993; Pracyk et al., 1995; Swada et al., 1980).

CO poisoning frequently results in neuropsychological sequelae, including cognitive, physical, and affective impairments. Survivors of CO poisoning may experience either...
persistent neurologic sequelae (PNS) or delayed neurologic sequelae (DNS). DNS is a clinical syndrome occurring after an initial period of recovery from an acute episode of CO poisoning (Dolan, 1985). Patients are normal or near normal for several days and then exhibit a marked deterioration in cognitive, affective, and/or neurologic function. The onset of DNS occurs from 2 to 40 days after the initial exposure to CO poisoning (Min, 1986; Myers, Snyder, & Emhoff, 1985). PNS occurs when individuals experience neurological and/or neuropsychological sequelae occurring immediately following CO poisoning that persist over time. The most frequently observed sequelae include: dementia, memory deficits, decreased attention, irritability, mood disturbances, personality changes, disturbances in gate, Parkinsonian-like symptoms, apraxia, visuo-spatial impairments, cortical blindness, convulsive disorders, and speech disturbances (Smith & Brandon, 1973; Thom & Keim, 1989; Thom et al., 1994). In addition to cognitive sequelae, affective changes have been reported following exposure to CO including depression (Bruno, Wagner, & Orrison, 1993; Chapel & Husain, 1978; Garland & Pearce 1967; Hopkins, Weaver, & Bigler, 1997; Jaeckle & Nasrallah, 1985; Jefferson, 1976), anxiety (Bruno et al., 1993; Hopkins et al., 1997; Jefferson, 1976), personality changes (Chapel & Husain, 1978), and emotional lability (Chapel & Husain, 1978).

The current article reports a severe case of acute CO toxicity that resulted in a 21-day coma. The victim was in a room in a residence, in which three other individuals died and a fourth individual was comatose for 14 days after the CO exposure. Serial neuropsychological testing was obtained along with neuroimaging, cerebral SPECT scans, and EEG studies.

**METHOD**

**Case Information**

Tom, the victim, was a 35-year-old right-handed White male college graduate employed as the lead systems level computer programmer for a multinational corporation based in the United States. Tom had a history of producing high level computer programs and programmed in three languages, including English, Chinese, and Japanese. Educational and vocational history were verified by a review of school and work records. He had no significant history of alcohol or illicit drug use. While visiting in the home of his parents on Christmas Eve of 1992, a furnace malfunction occurred during the night which produced high levels of CO in the environment. Five individuals in the room were exposed to extremely high levels of CO in the environment. Five individuals in the room were exposed to extremely high levels of CO, three of whom died. Tom and a brother were found unconscious. He was taken immediately via helicopter to a major medical center where he was admitted with a diagnosis of CO poisoning. On hospital admission, Tom was noted to be “comatose and unresponsive with decerebrate posturing and increased intracranial pressure.” A CT scan obtained several hours after admission, revealed diffuse cerebral edema without hemorrhage. An EEG the following day was abnormal and showed marked and diffuse generalized slowing. Four days later, a repeat brain CT scan demonstrated diffuse white matter encephalopathy with focal demyelination in the anterior commissure with mild ventricular asymmetry and a new lesion in the region of the right frontal horn.

Although Tom was placed on a ventilator with oxygen and subsequently received several hyperbaric oxygen treatments, he remained unresponsive in a coma for a period of 21 days. EEGs on 1/8/93 and 1/12/93, were abnormal with diffuse generalized slowing. His first MRI on 1/27/93 demonstrated multiple abnormal foci of increasing signal in both hemispheres with greater abnormalities on the left as opposed to right hemisphere.
MRI and mCi 99m Tc-HMPAO SPECT scans were done on 3/10/93. Following treatment on the ventilator and serial hyperbaric oxygen therapy, gradual improvement was seen and the patient became alert, approximately 22 days post-CO exposure. He was subsequently transferred to a rehabilitation hospital where he received neurocognitive therapy, from a board certified clinical neuropsychologist, and also received speech therapy, occupational therapy, and physical therapy.

Neuropsychological Tests

Three separate neuropsychological test batteries were administered using standardized administrations at 3 months, 1 year, and 3 years post-CO exposure (Bigler, 1988). The following tests were included on all three test sessions: Weschler Adult Intelligence Scale-Revised, Weschler Memory Scale-Revised, Wide Range Achievement Test, Category Test, Grip Strength, Finger Tapping, Trailmaking Test Parts A and B, and the Minnesota Multiphasic Personality Inventory-II. A variety of other tests were included with each test session by the different neuropsychologists who examined Tom, but the reported tests were the only ones common to all three neuropsychological exams.

Imaging Studies

MRI. MR images were acquired at 1.5 Tesla with a quadrature head coil using standard clinical protocols. Sagittal T1-weighted (500/11/2; TR/TE/excitations) images were first acquired followed by axial proton density and T2-weighted (3000/31; 90/1) spin echo images. Slice thickness was 5 mm with a 2-mm interslice space. Images were acquired on a 256 x 192 matrix with a 22-cm field of view for the axial images and a 24-cm field of view for the sagittal images.

QMRI. Axial dual-echo images were quantified as described by Blatter et al. (1995) using the software ANALYZE (Biomedical Imaging Resource, 1993). Quantitative or volumetric analysis of cerebral structures obtained from MRI were performed on all patients as per the methods described previously (Bigler et al., 1997; Blatter et al., 1995). Once volumes were obtained, such measures as ventricle-to-brain ration (VBR), a measure of diffuse atrophic changes, were compared to the normative database which allows comparisons to specific age and gender matched control groups. Other analyses included measurements of specific components of the ventricular system including temporal horns, third and fourth ventricles, total brain volume, and cerebrospinal fluid (CSF) volume. Measurements the hippocampi were also obtained. All ventricular and total brain volumes are reported as volumes in cubic centimeters (cm³).

SPECT. Regional Cerebral Perfusion Study images consisted of ninety-six 25-second images of the head obtained following IV administration of 25.0 mCi 99mTc-HMPAO (stabilized form). Visual and auditory stimuli were limited during injection and image acquisition. Planar images were recorded onto the computer for tomographic reconstruction using standard filtered back projection with ramp and Butterworth filters according to recommendations made by the camera manufacturer. Operational procedures conformed to the technical guidelines established by The Society of Nuclear Medicine Brain Imaging Council in 1996.
RESULTS

Neuropsychological Test Results

His first neuropsychological evaluation was completed on 3/15/93, 81 days postexposure. Table 1 summarizes the results of this evaluation for those tests that have been repeated over time. A demographic estimate of premorbid IQ indicates predicted WAIS-R scores of verbal = 118.5, performance = 113, and full scale = 117. By these conservative estimates (see Reynolds & Stanton, in press), there was clearly a substantial loss of overall intellectual function. Memory scores denote severe deficits with delayed recall particularly impaired and most scores in the severely impaired range. Even academic skills such as reading, spelling, and arithmetic were substantially below expectation given this patients age and educational background. Grip strength had deteriorated and a number of other nonspecific neuropsychological abnormalities were present. Beyond what is reported in Table 1, additional significant findings indicate a moderate level of impairment on the grooved pegboard, impairment on a line bisection task, difficulties with phoneme discrimination, and elevations on the MMPI-II on scales F, 1, 0, and 2.

Repeat testing nine months later (and nearly 12 months postinjury), 12/14/93, indicated some improvement in overall intellectual function, with an increase in performance IQ accounting for all of the improvement in intellectual function (refer to Table 1). Memory scores were increasing but were still significantly below normal, with the most pronounced difficulties remaining in the areas of attention and concentration. Academic skills show some improvement and his category test is within normal limits at this time. Grip strength declined but motor speed (finger tapping) had improved and there was a slight improvement in his performance on Trail Making but his scores remained significantly impaired (below the 5th percentile). Affective state shows significant deterioration as measured on the MMPI-II. The controlled oral word association test shows

### TABLE 1
Serial Test Results Following Severe Carbon Monoxide Poisoning on 12/24/92

<table>
<thead>
<tr>
<th></th>
<th>3/15/93</th>
<th>12/14/93</th>
<th>1/11/95</th>
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</thead>
<tbody>
<tr>
<td><strong>WAIS-R</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal IQ</td>
<td>89</td>
<td>87</td>
<td>96</td>
</tr>
<tr>
<td>Performance IQ</td>
<td>72</td>
<td>84</td>
<td>88</td>
</tr>
<tr>
<td>Full Scale IQ</td>
<td>79</td>
<td>84</td>
<td>93</td>
</tr>
<tr>
<td><strong>WMS-R</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal Memory Index</td>
<td>66</td>
<td>83</td>
<td>64</td>
</tr>
<tr>
<td>Visual Memory Index</td>
<td>76</td>
<td>93</td>
<td>67</td>
</tr>
<tr>
<td>Attention/Concentration Index</td>
<td>64</td>
<td>70</td>
<td>68</td>
</tr>
<tr>
<td>Delayed Recall Index</td>
<td>59</td>
<td>82</td>
<td>70</td>
</tr>
<tr>
<td><strong>WRAT-R</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reading</td>
<td>99</td>
<td>112</td>
<td>92</td>
</tr>
<tr>
<td>Spelling</td>
<td>86</td>
<td>97</td>
<td>94</td>
</tr>
<tr>
<td>Arithmetic</td>
<td>91</td>
<td>98</td>
<td>100</td>
</tr>
<tr>
<td>Category Test Errors</td>
<td>37</td>
<td>37</td>
<td>27</td>
</tr>
<tr>
<td>Grip strength (kg): right/left</td>
<td>43/33</td>
<td>30/32</td>
<td>53/55</td>
</tr>
<tr>
<td>Tapping Speed: right/left</td>
<td>50/45</td>
<td>70/59</td>
<td>45/41</td>
</tr>
<tr>
<td>Trail Making Test A/B (in seconds)</td>
<td>75/210</td>
<td>54/192</td>
<td>30/174</td>
</tr>
<tr>
<td>MMPI-II (scales above 65)</td>
<td>F,1,0,2</td>
<td>F,1,0,2,3,7,8</td>
<td>F,1,2,3,6,7,8</td>
</tr>
</tbody>
</table>

Note. WAIS-R = Wechsler Adult Intelligence Scale-Revised; WMS-R = Wechsler Memory Scale-Revised; WRAT-R = Wide Range Achievement Test; MMPI-II = Minnesota Multiphasic Personality Inventory-II.
performance at the 25th percentile which is also a stable deficit on subsequent testing 1 year later.

The third neuropsychological evaluation was conducted subsequent to the initiation of litigation and demonstrates improved intellectual function in verbal, performance, and full scale IQ approximately 13 months later on 1/11/95 (refer to Table 1). Memory performance declined significantly, to levels that were similar to those seen immediately after the initial injury. Academic scores show a decline in word reading but stability for spelling and arithmetic. Additional improvement was seen on the Category Test and grip strength. Tapping speed shows some decline and although his performance on the Trail Making Test showed some improvement, his performance was still abnormal. His affective state was essentially unchanged from the evaluation 13 months earlier and shows substantial difficulty with depression and confusion. The patient also had developed a characteristic gait disturbance that was believed to be due to delayed deterioration in basal ganglia function.

The patient was actively being treated for Major Depression with Zoloft but was notably unresponsive. Sleep initiation problems were present and related to the presence of obsessive, nonproductive, ruminative thought patterns. Episodic throbbing headaches continued to be reported and the patient complained subjectively of unclear thought processes, balance problems, decreased strength, difficulties with organizing work, irritability, impulsivity, increased anger, and inability to perform previous vocational activities. The patient was unable to balance his checkbook correctly and frequently made careless mistakes and he could not write even a simple computer program, as he tended to get confused by the logic used in programming.

Neuroimaging

Neuroimaging studies demonstrate generalized cerebral atrophy, manifested as increased sulcal space and ventricular dilation. Figure 1 shows an axial slice through the body of the lateral ventricles showing ventricular enlargement and a coronal slice showing cortical and hippocampal atrophy. Quantitative neuroimaging demonstrate bilateral hippocampal atrophy, enlargement of the lateral and III ventricles and a significantly increased VBR. Quantitative data are presented in Table 2. Quantitative brain MR imaging results are shown in Figure 2, wherein the data are presented by standard deviations from demographically matched normal, age and sex matched control subjects. Three-dimensional reconstruction of his brain reveals the extent of the ventricular enlargement and hippocampal atrophy compared to a normal control subjects (Figures 3–5) (for methods see Hopkins, et al., 1996). Cerebral perfusion studies (SPECT scan) show diminished perfusion in the right posterior parietal region and central photopenia which corresponds to the enlarged ventricular system. Figure 6 shows an axial SPECT slice showing marked central photopenia.

DISCUSSION

Carbon monoxide frequently causes a variety of cognitive impairments, including deficits in memory. Over time postinjury, this patient showed improving intellectual function, but impaired motor speed and significant memory impairments which showed little improvement over time. The decline in memory function, even following some initial improvement, may be related to delayed neurotoxic effects on the globus pallidus, caudate, and hippocampal regions. Neuropsychological testing has been shown to be sensi-
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tive to the effects of CO poisoning, and neuropsychological testing has demonstrated a variety of impairments in cognitive function. The neuropsychological data presented for Tom are consistent with previous reports which demonstrate negative effects of CO poisoning on psychomotor and cognitive functioning. Frequently reported cognitive impairments include impaired memory, mental processing speed, attention, visuo-spatial

TABLE 2
Quantitative Neuroimaging Data

<table>
<thead>
<tr>
<th>Neural Substrate (cm³)</th>
<th>Patient</th>
<th>M</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebrospinal fluid (CSF)</td>
<td>120.92</td>
<td>103.92</td>
<td>33.56</td>
</tr>
<tr>
<td>Subarachnoid CSF</td>
<td>84.71</td>
<td>86.50</td>
<td>32.01</td>
</tr>
<tr>
<td>Gray matter</td>
<td>819.70</td>
<td>699.59</td>
<td>77.51</td>
</tr>
<tr>
<td>White matter</td>
<td>508.50</td>
<td>645.99</td>
<td>88.22</td>
</tr>
<tr>
<td>Left temporal horn</td>
<td>0.03</td>
<td>0.03</td>
<td>0.16</td>
</tr>
<tr>
<td>Right temporal horn</td>
<td>0.03</td>
<td>0.02</td>
<td>0.16</td>
</tr>
<tr>
<td>Brain volume</td>
<td>1328.20</td>
<td>1345.58</td>
<td>33.56</td>
</tr>
<tr>
<td>Lateral ventricles</td>
<td>31.76</td>
<td>14.19</td>
<td>3.86</td>
</tr>
<tr>
<td>Third ventricle</td>
<td>1.90</td>
<td>0.67</td>
<td>0.19</td>
</tr>
<tr>
<td>Fourth ventricle</td>
<td>2.50</td>
<td>1.77</td>
<td>0.65</td>
</tr>
<tr>
<td>Total ventricle volume</td>
<td>36.21</td>
<td>17.04</td>
<td>3.87</td>
</tr>
<tr>
<td>Ventricle-brain ratio</td>
<td>2.73</td>
<td>1.27</td>
<td>0.30</td>
</tr>
<tr>
<td>Right hippocampus</td>
<td>1.41</td>
<td>2.77</td>
<td>0.27</td>
</tr>
<tr>
<td>Left hippocampus</td>
<td>1.29</td>
<td>2.64</td>
<td>0.32</td>
</tr>
</tbody>
</table>

FIGURE 1. Magnetic resonance (MR) images of the brain. The figure on the left shows and axial slice through the body of the lateral ventricles showing ventricular enlargement. The figure on the right shown a coronal slice though the hippocampus (arrow) showing hippocampal atrophy.
impairments, balance, and movement disorders (Winter & Miller, 1976; Yastrebov, Kurtov, & Razinkin, 1987). Similar findings have been reported by Jefferson (1976), who presents two case reports showing subtle neuropsychological and neuropsychiatric impairment that appeared over a period of months following recovery from acute CO toxicity.

Tom exhibited improvement in overall cognitive status as noted previously, but his memory skills failed to improve. Hippocampal involvement in memory function is a long-established finding in neuroscience and this finding is consistent with Tom’s decline.
Continuing Decline of Memory Following CO

The decline in memory function, even with some initial improvement, may be related to acute and delayed neurotoxic effects of CO on the medial temporal lobe and hippocampal regions. Hippocampal lesions may be found on CT or MRI following CO poisoning (Fife et al., 1980; Plum et al., 1962). Nabeshima et al. (1991) found significant cell loss of the CA1 pyramidal cells in the hippocampus of CO-poisoned rats. Not all individuals exposed to CO develop visible lesions on MRI. However, new quantitative MRI analysis are revealing previously unrecognized morphometric changes in these patients. A study by Hopkins et al. (1993) utilizing quantitative MRI analysis of the hippocampus in CO-poisoned patients with concomitant neurologic sequelae, revealed that the mean area of the hippocampus was significantly smaller than that of demographically matched control subjects. The subjects also exhibited significant memory impairments (Hopkins et al., 1993). Quantitative analyses show that Tom has marked hippocampal atrophy and ventricular enlargement compared to a normal control subjects. Similar results were found in a study of 13 CO-poisoned patients who had neuropsychological exams and quantitative brain MRI scans (QMRI) 1 year post-exposure. Of the 13 patients 62% had abnormal QMRIs with ventricular enlargement and increased VBRs, 62% had memory impairments and impaired attention in 38% (Gale et al., 1997).

Tom’s cerebral perfusion studies (SPECT scans) show diminished perfusion in the right posterior parietal region and central photopenia. Tom’s findings are consistent with previous SPECT studies in CO patients which show cerebral hypoperfusion deficits. One study found reduced regional cerebral blood flow in the frontal and temporal cortices in CO-poisoned patients (DeReuck et al., 1993). Similarly, Choi and colleagues reported diffuse hypoperfusion defects using SPECT scans in CO-exposed patients (Choi, Kim, Choi, Lee, & Lee, 1993). In addition, SPECT abnormalities 1 year posttrau-
matic brain injury were found to be a reliable predictor of poor clinical outcome (Jacobs, Put, Ingels, Put, & Bossuyt, 1996).

Tom exhibited abnormalities on an EEG 1 day postexposure showing marked and diffuse generalized slowing. A second EEG 11 months later, continued to show diffuse generalized slowing. Abnormal EEGs have been reported by other authors (Takahasi,

FIGURE 4. Sagittal three-dimensional view of the ventricles, hippocampus and fornix in a normal control subject compared to the patient. Note the ventricular enlargement and hippocampal atrophy following CO exposure.

FIGURE 5. Frontal three-dimensional view of the hippocampus and fornix in a normal control subject compared to the patient. Note the significant atrophy of the hippocampus and fornix following CO exposure.
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Kobayashi, & Sakabivara, 1978). Ducasse et al. (1988) reported that patients with moderate CO poisoning (no loss of consciousness, mean COHb = 24%) found the quantitative electroencephalograms and cerebral blood flow responses to acetazolamide were abnormal following exposure to CO.

Tom’s scores in the MMPI-II showed a number of elevated scales including the F (b), which Butcher (personal communication) reports to be a common finding among head injury patients, due to their decreased attention and concentration skills along with ease of mental fatigue. Over time he experienced increasing agitated depression which was unresponsive to Zoloft. Tom had increased irritability, impulsivity, anger and personality changes. Affective changes are frequently reported following CO exposure including depression (Garland & Pearce, 1967; Jaeckle & Nasrallah, 1985), personality changes and emotional lability (Chapel & Husain, 1978). One study in which normal control sub-

FIGURE 6. Transaxial view of a SPECT scan showing marked central photopenia which corresponds to the ventricular enlargement in the patient, following CO exposure.
jects were exposed to 8 hours of 100 ppm of CO, measured mood prior to and following the CO exposure. The authors found that subjects reported more depressed mood after the CO exposure (Groll-Knapp et al., 1982). A longitudinal study that followed 100 CO-poisoned patients for 1 year following CO exposure found that 66% of patients reported significant affective changes at 6 weeks, 44% at 6 months, and 39% at 1 year. Affective changes included depression, anxiety, irritability and decreased frustration tolerance (Hopkins et al., 1997). The mechanism(s) for the affective sequelae are unclear at the present time, but research in patients with pulmonary disease have noted a high incidence of mood disorders and personality change associated with hypoxia/hypoxemia (Guilleminault, Hoed, & Mitler, 1978; Prigatano, Parsons, Levin, Wright, & Hawryluk, 1983; Yellowlees, Alpers, Bowden, Bryant, & Ruffin, 1987). It has been hypothesized that hypoxemia may result in a disproportionate decline in dopaminergic cells which leads to reduced dopamine levels and mood disorders.

CONCLUSIONS

Quantitative neuroimaging clearly demonstrates generalized cerebral atrophy with specific atrophic changes in the hippocampus. This pattern of deficits is consistent with diffuse anoxic brain injury secondary to CO poisoning. Although neuroimaging studies demonstrated stable, neuropathological damage at the gross brain morphology level, memory performance was variable over time, actually demonstrating a subsequent drop-off after initial improvement. Standard psychometric intelligence as assessed by the WAIS-R demonstrated consistent, but modest improvement over time. This case study demonstrates the sensitivity of neuropsychological tests in detecting neurocognitive changes that cannot be predicted by neuroimaging studies alone. In addition, this case study illustrates the delayed degeneration of some brain structures which can occur following significant CO exposure.

Tom’s continuing depression and failure to respond to Zoloft, a selective serotonin reuptake inhibitor (SSRI), may be related to a disproportionate depletion of dopaminergic cells in the basal ganglia. Although we are unaware of research expressing a preference for SSRIs versus tricyclic antidepressants in treating depression post-CO poisoning, there are at least some functional and theoretical reasons to believe that tricyclic antidepressants that increase the utilization of dopamine instead of serotonin, may be more effective in such cases. The efficacy of tricyclic antidepressant medication following CO-induced depression, seems at least, a hypothesis worthy of empirical evaluation.

Two years postexposure, Tom continues to show CO-induced dementia, despite clear improvement in his overall IQs, that is likely related to diffuse generalized anoxia and other mechanisms. The memory deficits point to a degenerative effect of CO on the hippocampus and related structures. The gait disturbance, confirmed by MRI lesions in the basal ganglia, also point to the immediate and delayed effects of CO toxicity. Long-term follow-up through neuropsychological testing and neuroimaging is necessary to monitor patient status effectively following CO exposure. Proper rehabilitation planning can not occur without serial neuropsychological examination.

REFERENCES


