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Memory Disturbances Following Chronic, Low-Level Carbon Monoxide Exposure

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Neuropsychiatric sequelae are a common feature of acute carbon-monoxide (CO) poisoning—particularly when the patient has experienced an episode of CO-induced unconsciousness. In this case report, we present neuropsychological test data demonstrating the presence of mild cognitive impairments following a chronic (3-year) history of low-level CO exposure that never produced loss of consciousness. Deficits were limited to concentration and memory; performance on measures of general intelligence, visuospatial functioning, and speed and dexterity were well within the normal range.

Carbon monoxide (CO) poisoning has long been known to produce a variety of neuropsychiatric disorders. Although the exact nature and extent of symptoms varies significantly from person to person, most survivors show changes in personality as well as mild to moderately severe intellectual deterioration in the period following recovery of consciousness (Smith & Brandon, 1973; Chapel & Husain, 1978). Frequently these neurobehavioral disorders have a delayed onset, appearing suddenly after several days or weeks of what seems to be normal functioning (Choi, 1983; Min, 1986; Kitahara et al., 1974).

No distinctive neuropsychiatric syndrome has yet been identified as being unique to CO poisoning; indeed, clinical reports have repeatedly emphasized the fact that CO-induced anoxic lesions may trigger virtually any neurologic disorder, including amnesia (Spinnler et al., 1980), apraxia (Min,

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1986), visual object agnosia (Garland & Pearce, 1967), akinetic mutism (Smith et al., 1971), Parkinsonism (Jaeckle & Nasrallah, 1985), choreoathetosis (Schwartz et al., 1985), and peripheral neuropathy (Snyder, 1970). Nevertheless, memory and visuoconstructional disturbances tend to be the most prominent cognitive deficits, whereas depression and "affective incontinence," are the most frequently reported personality changes (Lacey, 1981; Garland & Pearce, 1967). Over time, the severity of these disturbances may reduce spontaneously, although complete recovery is rare. Of 63 patients followed by Smith and Brandon (1973) for an average of 3 years after acute CO poisoning, only 8 showed a significant improvement, whereas 27 noted that their ability to remember had worsened in the interim.

Because published reports of cognitive deficits are exceedingly rare in CO-intoxicated patients who have *not* experienced a loss of consciousness, one may be left with the impression that an episode of unconsciousness is a necessary condition for the emergence of neurobehavioral sequelae. For example, in one of the largest studies to date, Min (1986) found that only 10 of 738 patients (1.4%) admitted to the hospital with acute CO-Intoxication had no prior history of unconsciousness. Similarly, in all of the case histories cited by us thus far, every patient experienced loss of consciousness. Yet the possibility exists that the apparent relationship between the development of neuropsychiatric symptoms and the occurrence of CO-mediated unconsciousness is an artifact that merely reflects a bias in case ascertainment. That is, unconscious individuals are more likely to be brought in for a thorough medical evaluation, whereas individuals presenting with the vague, flu-like complaints of subacute CO intoxication (e.g., headache, irritability, dizziness) but without a history of unconsciousness, are liable to be dismissed as normal, or be misdiagnosed (Grace & Platt, 1981; Dolan, 1985).

Experimental (as opposed to clinical) studies of the neurobehavioral effects of *low-level* CO exposure on humans and animals have demonstrated that transient decrements in functioning occur frequently, and are correlated with both duration of exposure and CO concentration (for review, see Laties & Merigan, 1979). Given those observations, one might expect to find subtle cognitive impairments in humans who have been repeatedly exposed to low-to-moderate levels of CO, yet have never experienced an episode of unconsciousness. In this report we present neuropsychological test data demonstrating the presence of mild cognitive deficits in such a patient.

CASE REPORT

The patient is a 48-year-old right-handed married female who describes a 3-year history of constant headaches, lethargy, and memory problems. She reports that while she has no problem recalling events from the distant past,

she is having difficulty remembering new information, like addresses, appointments, and the gist of news stories, and has taken to carrying a small notebook to keep track of that information. She also states that she occasionally has periods of mental confusion such that "when I write or compose a paragraph I can't get it together." In addition to her memory problem, she also reports periods of depression, and is currently seeing a marriage counselor. She has attributed her depression and anxiety—at least in part—as a reaction to the development of her memory problems. Although she has never had an episode of unconsciousness, she reports that she nearly passed out once in her basement and as a consequence, had the gas company check her furnace. It was found to be releasing 180 ppm CO; this is more than 3 times the OSHA-mandated permissible level of CO (50 ppm). Although her headaches stopped after the appliance was replaced, she has continued to have memory difficulties. She was seen by us three months after her furnace was replaced. At no time were carboxyhemoglobin levels obtained from her.

This individual is a high school graduate who completed 2 years of business school. She worked for many years as a traffic dispatcher at a large warehouse complex. During the past six years she ran a typing service out of her home, doing most of the work in a basement room which also housed the furnace. It should be noted that her house is tightly insulated; in winter, very little outside air exchange occurs. She denies alcohol or drug abuse, has no past history of head trauma, no family history of psychiatric problems, and no known history of other toxic chemical exposures.

METHOD

A formal neuropsychological evaluation was carried out using the Pittsburgh Occupational Exposures Test (POET) Battery (Ryan et al., 1987). This collection of well-known cognitive tests includes several subtests from the Wechsler Adult Intelligence Scale (WAIS-R) and Wechsler Memory Scale (WMS), as well as a number of learning, memory, visuospatial, and visuomotor tests that have previously been shown to be sensitive to detecting impairments in groups of brain-damaged (Lezak, 1983) and occupationally exposed (Ryan et al., 1988) patients. In the initial normative study (Ryan et al., 1987), the POET was administered to 182 employed blue-collar males who had no previous history of toxic chemical exposures, or a previous history of neurologic or psychiatric disorder, or renal or heptic disease. Using those norms, it is possible to calculate for any individual a predicted score on each test which is adjusted for the effects of both age and education. In this way, one can determine how this individual's scores compare with other demographically similar, normal individuals. Although the normative data were collected only from men, other investigators (Filskov & Catanese, 1986; Heaton et al., 1986) have failed to find significant differ-

ences between men and women on the types of tests comprising the POET battery.

RESULTS

POET test scores from our patient are summarized in Table 1. Formal testing reveals an individual of "average" intelligence who is currently performing well within the "average" range on all measures *except* those tests measuring new learning ability and memory for recently studied information. Several of her performances are particularly noteworthy. For example, the Incidental Memory Test is administered immediately after the subject completes the WAIS-R Digit Symbol Substitution Test and requires subjects to recall the 9 digit-symbol pairs. Most subjects readily recall 6 or 7 of the 9 pairs; our patient recalled only 2 of the 9—a score that falls in the lowest fifth percentile of the normative distribution. Our patient also performed at the fifth percentile on the Recurring Words test. On this continuous recognition test, a series of 4-letter abstract words (e.g., love, wise, much) are visually presented with some (18 words) shown only once, while others are

TABLE 1
Summary of Neuropsychological Test Scores

General Intelligence: WAIS-R Subtests (Age-Scaled Scores)

Information	9	Picture Completion	7
Similarities	15	Block Design	10
Digit Span	11	Digit Symbol	11

Learning and Memory

	Verbal Learning (10 possible)	Symbol-Digit Learning (7 possible)
Trial 1	0	3
Trial 2	2	4
Trial 3	7	4
Trial 4	9	6
Delayed Recall	4	7

Visual Reproductions (17 points possible) -Immediate Recall: 7
Delayed Recall: 5

Incidental Memory (9 possible): 2
Recurring Words (50 possible): 38

Eye-Hand Coordination and Mental Flexibility

Trail Making-Part A: 27 seconds
Part B: 75 seconds
Grooved Pegboard-Dominant Hand: 80 seconds
Nondominant Hand: 70 seconds

MMPI *T* Scores

Scale:	L	F	K	1	2	3	4	5	6	7	8	9	0
Score:	66	58	62	89	78	98	62	32	82	83	91	68	55

repeated (16), presented 3 (2), 4 (1), or 6 (1) times. Most subjects find this task quite simple; and on the 50 trials, typically make an average of 44 or more correct identifications. In contrast, our patient made 12 errors, all of which were false positives; that is, items she had seen previously were misidentified by her as "new."

Relatively poor performances were also obtained on two paired-associate learning tests. On the Verbal Learning Test, a task that requires the subject to learn a list of 10 pairs of unrelated words (neck/salt), our patient showed evidence of learning over the 4 study/test trials, though she never mastered all 10 pairs, and her overall rate of learning fell in the lowest 25th percentile of the normative sample. It is interesting to note that while she had no difficulty using associative mnemonics to link the to-be-remembered words (i.e., her ability to encode new information appears to be intact) she had a great deal of difficulty retrieving the appropriate response word when cued with the stimulus term. This was most evident on the delayed recall task. For example, 30 minutes after learning the word pair "silk/pine" she was cued with "silk" and responded, "palm, – not a cone, – something to do with a tree." For the pair "gate/native" she responded "foreign – not a foreigner" when cued with the word "gate." As a consequence, unlike most normal people who, when evaluated after a delay, are able to recall nearly as many items as they learned initially, our patient was able to remember less than half of the word pairs she had previously mastered – a performance that falls in the lowest quartile. This deficit cannot easily be attributed to a word-finding difficulty, for not only did she show no clinical evidence of dysnomnia, but she performed normally on a cued word retrieval task (the Controlled Oral Word Association Test; Benton & Hamsher, 1976), earning a score on that which falls in the upper 25th percentile, according to the Benton and Hamsher norms. Associative learning ability was also assessed with the Symbol Digit Learning Test, a test on which the seven to-be-remembered items consist of meaningless symbols paired with single digits. On this task, she performed somewhat better than on the verbal learning task, though again, her overall rate of learning fell in the lower end of the normal distribution.

Both short- and long-term visual memory processes are also significantly impaired in this patient. This was most apparent on our modified version of the Visual Reproductions subtest from the Wechsler Memory Scale. We have modified that test in two ways. First, following the immediate recall test, the subject is asked to copy each design; 30 minutes later, a delayed recall is requested. Second, the scoring criteria have been modified such that an additional "accuracy point" is added for each design. These changes are described in more detail elsewhere (Ryan et al., 1987). We found that immediately after studying each of the designs, our patient tended to omit, or misplace crucial design elements. When retested after a 30-minute delay, she

was able to recall only 3 of the 4 designs, and 2 of those bore only a slight resemblance to the original models. This is particularly surprising because following the immediate recall test, she was given an opportunity to copy each design accurately. As a consequence, her poor performance on the delayed-recall test cannot be attributed to a failure of attention, perception, or motor coordination.

In cases of this sort, where there is a possibility of litigation, we are concerned that patients may be "malingering," or otherwise exaggerating the severity of their impairments. For that reason, we routinely administer a task that we have previously found to be sensitive to "faking bad." We have modified the Best Answer Form of the Benton Visual Retention Test [Form F] such that suggestible subjects are "given permission" to perform poorly. After completing a series of challenging tests the subject is told that "many people find this next task to be quite difficult but we want you to try your best; you'll see a design for *only 5 sec* and then it will be removed and you'll have to select it from a set of 4 designs." Individuals who perform extremely poorly on this measure (score of 9 or less of 15 possible) but perform relatively well on other measures, like Digit Span, are considered to be exaggerating the severity of their impairment. On that task, our patient performed well within the "normal" range. She also indicated that she was not now involved in litigation, and had no plans to initiate a lawsuit.

To examine current personality functioning, we administered the MMPI, and obtained a clinically elevated profile having the following Welsh Code: 38*176:2;94-0/5# LK-F/. This profile is consistent with our patient's complaints of chronic subjective distress, her feelings of depression and anxiety, her complaints of memory problems and mental confusion, and her series of nonspecific physical symptoms that include dizziness and headaches.

DISCUSSION

There is no doubt that this patient has developed a clinically significant memory disorder. Prior to her exposure she worked in positions that placed heavy demands on concentration and memory skills; following this exposure, she was unable to keep track of verbal information that had been presented seconds earlier, and had difficulty accurately retrieving both verbal and visual information that she had learned within the past 30 minutes. These deficits are relatively circumscribed, insofar as she performed within the average range for someone of her age on most other tasks, including measures of general intelligence, visuospatial functioning, motor speed and eye-hand coordination, and verbal and nonverbal problem solving.

Several possible explanations for these results come to mind. Because it is widely believed that depressed individuals show serious cognitive dysfunction, it is tempting to attribute our patient's memory dysfunction solely to

her affective disorder. Unfortunately, there is little empirical evidence in the literature that middle-aged, mildly depressed, unmedicated individuals manifest serious memory problems (e.g., Friedman, 1964). Moreover, when memory disorders are found in depressed patients, they tend to reflect encoding problems (Weingartner et al., 1981) and tend to be associated with motor slowing (Cohen et al., 1982). Our patient's memory problems seem to reflect a disorder of retrieval, rather than an encoding dysfunction, since she had little difficulty using sophisticated associative mnemonics to learn a list of unrelated word pairs. Furthermore, she showed no evidence of mental or motor slowing on a wide range of information-processing tasks.

Several other, very common causes of neuropsychological dysfunction include chronic alcohol abuse and head injury, as well as a variety of other psychiatric, neurologic and biomedical disorders (Tarter et al., 1988). Again, we find no compelling evidence that our patient's performance decrements are a consequence of any of those agents. She reports no previous history of even moderate social drinking, nor has she ever experienced any sort of head trauma. Neither she, nor anyone in her immediate family, report any history of a previous neurologic or psychiatric disorder. Similarly, she has no history of a medical disorder (e.g., hypertension, liver or kidney disease) that could compromise neuropsychological functioning.

While we cannot completely rule out the possibility that she is in the earliest stage of a rare medical disease that disrupts memory, it is more parsimonious to attribute her relatively isolated neuropsychological disturbance, her affective disorder, and her somatic complaints to her three-year history of low-level carbon monoxide exposure. The absence of CO-induced unconsciousness, as well as the failure to obtain carboxyhemoglobin levels during her period of exposure make it impossible for us to *unequivocally* attribute her deficits to CO. Nevertheless, in the absence of any other etiologic agent, we find that chronic CO provides the most reasonable explanation for her pattern of symptoms. Support for this conclusion comes from several converging sources. First, our patient's furnace was found by the gas company to be emitting unusually high levels of CO; an extensive literature has indicated that faulty gas appliances may produce excessive CO levels that can eventuate in poisoning (e.g., Grace & Platt, 1981; Jaeckle & Nasrallah, 1985; Snyder, 1970; Spinnler et al., 1980). Second, relatively low levels of CO exposure are known to produce both the mild somatic complaints (headaches, lethargy), as well as symptoms of depression and anxiety similar to those reported by our patient (cf. Dolan, 1985). Third, memory disturbances are one of the most frequently reported cognitive changes reported following an episode of CO poisoning (Min, 1986). In fact, Spinnler and associates (1980) have reported a memory disorder in a CO-poisoned patient that is nearly identical to that seen in our patient—that is, characterized primarily as a disorder of retrieval.

The association between a faulty gas appliance and changes in memory, concentration, and mood were made by our patient only after an incident when she was nearly stuporous from the exposure. Although she had previously sought medical treatment on a number of occasions, her nonspecific complaints were repeatedly dismissed, with diagnoses ranging from flu to conversion hysteria. These diagnostic errors are certainly not surprising, and probably not uncommon, because our patient did not manifest the "typical" CO-poisoning profile. Not only did our patient have no prior history of unconsciousness, but she also had no obvious evidence of CO exposure: she had not attempted suicide, and did not work in an environment where high CO levels are expected (e.g., garage; mine).

This case suggests that a loss of consciousness is not necessary for the development of neuropsychiatric symptoms following a period of CO exposure. Unfortunately, in the absence of a large-scale prospective study of individuals chronically exposed to low levels of CO, it is impossible to determine which exposure parameters (e.g., duration, dose) are most likely to eventuate in impairment. From a clinical perspective, this report suggests that changes in affective state accompanied by complaints of concentration and memory disorder do not necessarily indicate the onset of a psychogenic depressive disorder. Rather, such symptoms may reflect the occurrence of mild CNS changes triggered by chronic, low-level exposure to toxic pollutants.

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