CASE REPORT

Persistent cognitive and motor deficits following acute hydrogen sulphide poisoning

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This case study describes the long-term after-effects of hydrogen sulphide exposure in a previously healthy 27-year-old male. Upon hospital admission the patient had a Glasgow Coma Score (CGS) of 3; with emergency treatment including hyperbaric oxygen treatments, he progressed to a GCS of 15 on day 7. Although both CT and MRI scans were unremarkable, PET using F-18 deoxyglucose administered 3 years after the accident showed abnormally decreased metabolism bilaterally in the temporal and inferior parietal lobes as well as the left thalamus. Uptake in the striatum was heterogeneous and abnormal. A cerebral perfusion study using SPECT performed 3.5 years after the accident revealed bilaterally decreased flow in the putamen but no cortical abnormalities. Neuropsychological and neurofunctional testing revealed the following impairments: microsmia, psychomotor slowing, extrapyramidal signs and deficits in memory and executive/planning functioning. These findings are discussed in the context of hydrogen sulphide’s known mechanisms of toxicity and the functions of the basal ganglia.

Key words: Basal ganglia; executive functions; hydrogen sulphide; striatum.

INTRODUCTION

Hydrogen sulphide, a colourless gas with the odour of rotten eggs, is commonly found in the presence of degrading protein waste. It is a by product generated in several industries and is also present in sewers ('sewer gas'), cesspools and wherever putrefaction takes place. Despite its distinctive odour, smell is not a dependable way to detect this gas because it rapidly paralyzes olfactory nerve endings at high (dangerous) concentrations.1 The proposed safe air concentration of hydrogen sulphide is 10 ppm.2 At low to moderate concentrations (50–200 ppm), toxic symptoms are due chiefly to local tissue irritation. Exposure to concentrations greater than 300 ppm can produce respiratory depression, tremors, coma, cyanosis, convulsions and tachycardia.3 Concentrations above 1000 ppm are usually fatal after a few minutes;4 a few breaths at this concentration typically leads to abrupt loss of consciousness and, if exposure is not terminated rapidly, death.

Hydrogen sulphide, with a mechanism of action similar to cyanide,1 poisons metallo-enzymes, particularly mitochondrial cytochrome oxidase, thereby preventing cells from using oxygen.1 Fatal poisoning causes greenish discoloration of the brain, particularly the cerebral cortices and the basal ganglia,4 while low density areas on computed tomography scans have been observed in the basal ganglia and surrounding white matter in
both chronic and fatal hydrogen sulphide exposures.\(^5,6\) Exposure to high concentration of hydrogen sulphide causes headache, nausea, dizziness, confusion, weakness and loss of consciousness. Although the neurological problems of hydrogen sulphide exposed survivors have been documented (e.g., intention tremor, neurasthenia, balance problems) relatively little is known about neurobehavioral abnormalities in these patients. This report details extensive neurofunctional testing, together with morphological and functional imaging studies, on a construction worker who ‘recovered’ from hydrogen sulphide poisoning.

**CASE REPORT**

The patient was a previously healthy 27-year-old male construction worker. Throughout grade school, he was a popular, well-adjusted, conscientious student who performed at or above grade level on achievement/academic indices. He attended and graduated from a vocational high school with a major in auto mechanics. He received excellent or outstanding grades in categories such as achievement, punctuality, ambition, learning experience and quality/quantity of work and graduated with a 3.0 grade point average. After graduation he worked on construction-related jobs and was well-known locally for his work as a designer and builder of Monster Trucks.

The patient was working with a construction crew that was building a sewer system on a strip of New Jersey wetland approximately 500 yards from the Atlantic Ocean. Hydrogen sulphide exposure occurred in a 27-foot-deep pit in which the men were working; gas concentration was not specified. The patient was overcome as he was descending a ladder into the pit to rescue a co-worker. He fell an unknown distance and there was no evidence of head trauma (i.e., absence of skin abrasions or bruising, normal head CT). There is no indication that the patient had stopped breathing at any time. A police officer attempting to rescue these men was also overcome by fumes and died at the scene. The patient and the other worker were rescued and transported to local hospitals. The other worker was treated with hyperbaric oxygen and released from the hospital 48 h later. This person has not been available to us for follow-up testing; long-term sequelae, if any, are unknown.

After extrication from the site, the patient was transferred to a local trauma centre where he was admitted with a Glasgow Coma Score (GCS) of 3, heart rate 122 beats/min, sinus tachycardia, blood pressure of 130/65 mm Hg, respiration 16 breaths/min and pupils dilated and sluggish. At the scene of the accident the patient was reported to have had seizures, but this could not be verified. Upon arrival in the emergency room, seizure activity and decerebrate posturing were described. Temperature was 101.2° F and carboxyhemoglobin was 14.9%. No spontaneous movements were noted, corneal reflexes were absent and deep tendon reflexes were 2/4. A body CT scan showed pulmonary oedema while a head CT scan was normal.

The patient was transferred to a hyperbaric medicine unit (approximately 10 h after exposure) where he received 300 mg of sodium nitrite, 20 mg furosemide and 10 mg vecuronium and was started on hyperbaric oxygen treatments (2 atmospheres oxygen for 45 min) b.i.d. for the next several days. Five days after admission he regained consciousness and could respond to simple commands. His neurological status improved to a GCS score of 11 and on day 7, after his GCS score improved to 15, hyperbaric oxygen treatments were discontinued. The patient was able to feed himself and ambulate with assistance. However, he was agitated and restless and had impaired language, memory and attention.

The patient entered a rehabilitation facility sixteen days after hospital admission. He was found to have slowed speech, impaired attention span, retrograde amnesia with confabulation, decreased insight and ability to communicate, flat affect and impaired visual memory with poor acquisition, retention and recall of new information. On leaving the rehabilitation facility after approximately one month, neuropsychological evaluation revealed difficulty on verbal and visual memory tasks and associative learning. The patient required cueing in order to carry out simple jobs involving rudimentary planning, organizing and sequencing. The discharge summary also noted that there were left-sided deficits in balance and speed of movement. Over the four years since the accident, the patient is noted by family and health professionals to have continued problems with short-term memory, sequential thinking, decreased attention and lack of initiative.

A follow-up brain MRI scan performed 17 months after the accident showed no evidence of abnormal signal, mass, midline shift or sulcal effacement. The posterior fossa, base of the skull and all visible structures appeared normal. In contrast, a positron emission tomography (PET) scan using F-18 deoxyglucose performed 3 years after the accident, showed markedly decreased metabolism in the left thalamus, heterogeneous and abnormal uptake in the basal ganglia, and abnormally decreased metabolism in both temporal and inferior parietal lobes. A cerebral perfusion study (SPECT scan) performed 3.5 years after the accident revealed bilaterally decreased activity in the putamen and the amygdala/hippocampal region but no cortical perfusion abnormalities (Figure 1). Another brain MRI scan performed one month after the SPECT scan was unremarkable showing no evidence of basal ganglia lesion.

**Evaluation of functioning**

The present neuropsychological evaluation took place over three sessions approximately 4 years after the accident. In the first two sessions, the patient received a full neuropsychological and neurofunctional test
Figure 1. A cerebral perfusion study was conducted approximately 3.5 years after the accident. SPECT images of the brain were acquired about one hour after the intravenous administration of 740 MBq (20mCi) of Technetium-99m (Tc-99m) labelled HMPAO (Ceretec, Amersham Intl., Arlington Heights, II) on a triple headed camera equipped with fan beam collimators (Picker Intl., Cleveland, OH). The intrinsic resolution of the camera was rated at about 8-9 mm full width half maximum. The back-projected images were reconstructed with a count rate dependent restoration filter. The modulation transfer function was generated from the line spread function of the camera. Chang's method was used to correct the SPECT scans for attenuation with a uniform ellipse. The findings were assessed with a reference to a normal data base of 44 healthy volunteers. A shows a SPECT from a neurologically intact individual and B shows the subject of the present case report. Decreased activity was demonstrated in the putamen, and the amygdala/hippocampal region bilaterally with the greatest effect in the right hemisphere. Arrows indicate the striatum.

battery as described below. At that time he was receiving no medications. At the final test session 9 months later, the efficacy of pharmacotherapy (Cylert and Ritalin) was evaluated by retesting with several of the tests that the patient had shown most difficulty performing in the unmedicated state (see ‘Effects of medication’).

General cognitive abilities
The patient was alert, calm, co-operative and well-oriented to place and time. Due to his memory problems the patient was a poor historian so that relevant details of medical background could only be provided by his spouse. Despite his inability to recall salient events in his past, the patient was seemingly unaware and unconcerned about his disabilities. When queried about his difficulties, he replied with equanimity that ‘I’m told that I have memory problems’. Despite the reports by his wife of the beneficial effects of medication on his behaviour, he could see no advantage in continuing to take his pills. Affect was blunted; when questioned about his current state in which he is no longer able to sustain employment, he neither exhibited nor expressed either distress or anxiety. The patient was not depressed (Beck Depression Inventory score = 0) and showed no signs of dementia (Mini Mental State Exam score = 27). The University of Pennsylvania Smell Identification Test (UPSIT) showed the patient to be microsmic, correctly identifying only 31 of 40 odour stimuli. Confrontational naming ability was intact, as assessed by a 15-item version of the Boston Naming Test. Pre-morbid verbal IQ was estimated at 100.2 based on the National Adult Reading Test (NART). Performance on the Information Subtest of the WAIS-R resulted in a percentile ranking of 16. This test is reported to measure ‘... general ability, that ubiquitous test factor that appears to be the statistical counterpart of learning capacity plus mental alertness, speed, and efficiency’.

Motor functioning
Motor testing included a standard neurological exam, assessment on the motor portion of the Unified Parkinson’s Disease Rating Scale (UPDRS), and computerized human performance measurements designed to precisely assess biophysical parameters of movement, such as movement speed and accuracy, using computer-controlled biomechanical transducers. The patient’s neurological exam was unremarkable. Strength, muscle tone and bulk, range of movement, posture, balance, gait, cranial nerves and somatosensory processing appeared grossly normal. The UPDRS detected no unambiguous signs of Parkinsonism, however, isolated extrapyramidal signs were noted. In particular, progressive slowing (early fatigue) was
noted during performance of repetitive hand or leg movements, punctuated by hesitations or abrupt arrests of movement.

Human performance measurements revealed abnormal functioning in several domains. The speed of simple repetitive movements such as flexion/extension (tapping) of index finger (4.1 taps/sec), and ankle (3.6 taps/sec) as well as reaching movements with the arm or leg were significantly slowed as compared to healthy individuals of similar age.

Deficits were also observed on several visuomotor tasks. Visual information processing speeds were significantly slowed during performance of visuomotor tasks compared to age-matched individuals with no neurological impairments. Movement accuracy and co-ordination were assessed and right arm co-ordination was significantly impaired compared to intact individuals.

Cognitive functioning

The patient reported experiencing difficulty in remembering recent events and current information and complained of difficulty in performing tasks that require several related steps for completion. He also claimed to have decreased energy and initiative and difficulty in concentrating on tasks.

Visual-spatial functions were tested by the picture completion and block design subtests of the Wechsler Adult Intelligence Scale — Revised. The subject scored in the 91st percentile on picture completion and the 75th percentile on block design. On the Stroop Word–Color Test, the subject scored 45 (age-matched norm = 44.7) on the colour–word segment indicating no deficit in the ability to ward off distraction. Similarly, analysis of attention with Conner’s Continuous Performance Test also was within normal limits.

Memory function was assessed by administering the Wechsler Memory Scale Revised test battery. Visual memory as measured by the Visual Memory Index was superior (~75th percentile) while verbal memory (Verbal Memory Index) (~10th percentile) and the patient’s General Memory Index (28th percentile), a composite of the visual and verbal indices, were lower than would be expected for someone with his premorbid levels of functioning. In addition, long-term storage was impaired with the Delayed Recall Index in the lower 5th percentile.

Memory and attention were also assessed using the computerized Cambridge Automated Neuropsychological Test Battery (paired associate learning, visual pattern recognition memory, spatial recognition memory, delayed matching-to-sample and attentional set shifting capacity). For these tests, the patient sat in front of a touch sensitive computer monitor and made all responses by touching the appropriate stimulus on the monitor. These tests are described in detail elsewhere and discussed briefly in the following paragraphs.

In the paired associate learning test, the subject was required to learn a set of pattern–location associations varying in number from 1–8. The test started at a simple level and became more complex with later sets of stimuli. In the pattern recognition test, the subject was presented with a series of abstract patterns in the centre of the monitor. Each stimulus was presented for 3 sec and 12 stimuli were presented in a block. Five sec after the end of the block the subject was required to choose between the pattern he had already seen and a novel pattern by pointing to the former. In the spatial recognition test, the subject had to remember specific locations of stimuli on the screen. For performance of delayed matching-to-sample, the subject was shown a complex abstract pattern in a box in the centre of the monitor and was required to match it to one of four choice patterns shown underneath the sample. One of the choice patterns was identical to the sample, one was a novel distractor pattern, one had the shape of the sample but the colours of the distractor, and the fourth had the colour of the sample and the shape of the distractor. The matching stimuli were presented either with the sample (simultaneous match), immediately after (0 sec delay) or 4 or 12 sec after the sample stimulus was extinguished.

In the attention set shifting task, the subject was required to learn a series of discriminations in which one of two stimuli was correct and the other was not, using feedback provided by the computer. The subject was presented with up to eight stages of the task with increasingly difficult task solutions. In order to advance to the next stage, the subject had to learn the discrimination to a criterion of six successive correct responses. Once this was achieved, the computer automatically advanced to the next stage, and the subject had to learn the new rule to keep on producing correct responses, although the subject was not explicitly told that the contingencies had changed.

The subject had no apparent difficulty performing the paired associate learning task, successfully completing the most difficult level of the task requiring the learning of eight pattern–location associations. Pattern recognition memory was normal with the subject scoring 23 correct responses and only one incorrect response. In contrast, spatial recognition memory was impaired, with the subject recording only nine correct responses out of 20 trials (1st percentile). The subject also was impaired on the delayed matching-to-sample task showing more errors at longer delay intervals, a pattern indicative of working memory dysfunction. The subject had no difficulty in performing the attention set shifting task, successfully completing all stages.

An automated version of the Tower of Hanoi execu-
tive function/planning task was also administered. On this test of planning ability, the subject must place blocks of different sizes in ascending size order on a pedestal located between two other pedestals. A larger block cannot be placed on top of a smaller block. To solve this task, one must identify alternative strategies, choose the best approach and conceive the most efficient hierarchical sequence of moves. The faster the subject performs the task and the fewer the moves taken to finish the higher the score. Performance on this task was clearly abnormal, indicating a significant problem in planning abilities. The subject correctly solved only four out of nine puzzles and had no perfect solutions (i.e., solved the puzzle in the minimum numbers of moves). His mean score was 790, considerably lower than that achieved by intact individuals (1st percentile). In addition, the average time taken per move (thinking time) was significantly slowed and more variable (10.59 ± 7.5 sec) than in a control population (3.69 ± 0.70 sec).

**Effects of medication**

A variety of medications were administered in an attempt to ameliorate some of the symptoms experienced by this patient. The combination of Cylert and Ritalin were subjectively felt by the patient to give him ‘energy’. Drug doses were raised systematically to effect. The optimal doses were 112.5 mg of Cylert b.i.d. and 20 mg of Ritalin q.i.d. Despite the high doses of these drugs, liver profiles remained normal. Most responsive, in both the opinion of the patient and also his care givers (i.e., spouse, occupational therapist), was his striking lassitude. In the unmedicated state, the patient was content to sit idly or, with prodding, to wash the dishes, vacuum or do the laundry. His wife reported that after he received these drugs the patient showed some initiative, for example, in performing simple household chores without being prompted.

Assessment in the medicated state was confined to several tests with which the patient experienced difficulty in the initial evaluation. No changes were shown in tests of either spatial memory or visual working memory; the patient remained severely impaired. In contrast, speed of movements involving the digits, arms or legs showed a small but consistent increase (mean improvement for all movements = 12.75% ± 7.7). A more striking improvement was seen in planning ability as evidenced by performance on the Tower of Hanoi task. The patient solved more puzzles than when unmedicated (77% vs. 44%) and in a more efficient fashion elevating his percentile ranking from the 1st to the 41st percentile. In addition, slowing of central processing appeared to be somewhat ameliorated by drug treatment in that the patient’s average time per move in this task dropped from 10.59 to 4.78 seconds. It should be noted that different puzzles that were equated for degree of difficulty were used in the two sessions.

**CONCLUSIONS**

Neuropsychological and neurofunctional testing of this subject revealed the following pattern of deficits: microsmia, motor slowing, slowing of central information processing, memory deficits and executive function/planning deficits. One apparent discrepancy in memory test results bears mention. The Visual Memory Index of the WMS-R showed above average performance while the spatial recognition and delayed matching to sample tests of the Cambridge Automated Neuropsychological Test Battery indicated severe impairment. The seeming contradiction between these results is probably more apparent than real. The components of the WMS-R that contribute to the Visual Memory Index have been criticized as an inadequate assessment of visual memory.

This patient’s pattern of neurobehavioral impairments is in accord with the abnormal findings on functional scans. The wide spectrum of memory problems detected are consistent with the indications of dysfunction in three areas that have been heavily implicated in the storage and retrieval of memory (frontal lobes, temporal cortex and striatum). Slowing of central information processing speed (bradyphrenia), motor slowing and the presence of isolated extrapyramidal signs are hallmarks of striatal dysfunction. Planning deficits are also indicative of striatal dysfunction and disruption of striatal-frontal cortical circuits.

Despite the memory and executive function deficits noted, attention and attention set shifting, in particular, appeared to be relatively intact. The subject could effectively shift attention away from previously relevant dimensions when they became irrelevant and could refocus his attention on newly relevant dimensions. This suggests that frontal attentional circuits were functional and that the striatal dysfunction, which appeared to be centred more in the putamen than the caudate nucleus, did not significantly impair function- ing of those fronto-striatal circuits involved in this behaviour.

The spectrum of deficits noted in this individual, especially those that seem to involve basal ganglia dysfunction, are consistent with the effects of hydrogen sulphide on the brain. Hydrogen sulphide inhibits oxidative phosphorylation and impairs mitochondria energy production thereby causing oxidative stress. The basal ganglia, particularly its dopamine system, are highly susceptible to oxidative stress and impaired metabolism. Another mitochondrial poison, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), destroys dopamine neurons and produces many of the features of Parkinsonism, including cognitive dysfunction. These cognitive deficits can appear after low level exposure, even in the absence of overt Parkinsonian motor signs. It is therefore noteworthy that Ritalin, a drug that enhances dopaminergic functioning, and Cylert, a drug with actions presumed to be similar to those of Ritalin, positively affected some of the
patient's symptoms. However, if the patient's dopamine system has indeed been compromised, further deterioration is plausible. Dopamine levels may decline with ageing though not typically to levels that compromise functioning. However, if this patient's dopamine system is already damaged, his risk of subsequently developing Parkinson's disease may be elevated.

The picture that emerges from neuropsychological testing is of an individual with a variety of problems such as bradyphrenia, poor memory and impaired planning ability. However, this list of deficits fails to convey the actual impact of this toxic exposure on this patient's life. Observations by the psychiatrist he has been seeing since the accident are necessary to complete the portrait. 'He frequently, in this interview, deferred judgement issues to his wife for her decisions because he realizes he is not able to adequately function independently. He shows overt contradiction, sees the overt contradiction in his comments, and yet cannot integrate the contradictory thinking. For example, he indicates to me that it made sense for the state to take his license because he is unable to react appropriately as he drives; however, it makes sense for him to drive when they return his license. He sees the contradiction but does nothing with it; he just shrugs his shoulders and says he is fine. He does not report any independent activities that are sustained in any manner, shape or form. He describes essentially a totally goal-less existence'.

REFERENCES