Digit and letter alexia in carbon monoxide poisoning

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Abstract
This study examined a 24-year-old patient with delayed encephalopathy, who was admitted to hospital with complaints of headache and visual impairment 1 week after acute carbon monoxide poisoning. The results of a visual field assessment, electroencephalography and head magnetic resonance imaging indicated damage to the cerebral cortex. After a 2-week treatment period, the patient had recovered from the visual impairment, but exhibited digit- and letter-reading difficulty. The Chinese aphasia battery and the number and letter battery supplement were conducted. The results revealed that the patient exhibited digit and letter alexia, while the ability to read Chinese characters was preserved. In contrast, the patient exhibited a deficit in Chinese character writing, while number and letter writing remained intact. Following treatment, reading and writing ability was improved and electroencephalographic abnormalities were ameliorated. Overall, our experimental findings demonstrated that delayed encephalopathy following acute carbon monoxide poisoning was characterized by digit and letter alexia.

Key Words
carbon monoxide; delayed encephalopathy; digit alexia; letter alexia; poisoning; neural regeneration

Research Highlights
A case of delayed encephalopathy, presenting with headache and visual impairment after acute carbon monoxide poisoning, was examined.

INTRODUCTION
Carbon monoxide poisoning is the fourth most common type of poisoning in China¹, and is a leading cause of neurological disturbances². The psychiatric and neurological symptoms of carbon monoxide poisoning include headache, muscle weakness, drowsiness, memory disturbances, apraxia, delirium, speech disorder, epileptic seizure, ataxia, and symptoms of Parkinsonism³–⁵. Most symptoms are non-specific, and some appear after a delay period⁶–⁸. Nevertheless, selective alexia has seldom been documented. The causes of dyslexia are poorly understood, but have been linked to damage to a reading-specific brain region in the left hemisphere known as the visual speech area. In this study, we describe a case of delayed encephalopathy with digit and letter alexia following carbon monoxide poisoning.

CASE REPORT

General patient information (Table 1)

Diagnosis
The patient was diagnosed with delayed encephalopathy after acute carbon monoxide poisoning. Treatments included...
hyperbaric oxygen therapy, as well as a low dose of methylprednisolone (80 mg a day) and drugs for neurotrophism. This project was approved by the Administrative Regulations on Medical Institution, formulated by the State Council of the People’s Republic of China<sup>11</sup>. Written informed consent was obtained from the patient prior to the study.

At admission, the patient complained of visual impairment, as well as digit and letter alexia after acute carbon monoxide poisoning. All symptoms appeared to be related to cortical injury. Other common diseases that cause acute focal cortical injury include stroke (ischemia and hemorrhage), trauma, and metabolic diseases (such as mitochondrial encephalomyopathy). Li et al.<sup>12</sup> reported a case of digit alexia after left parietal lobe hemorrhage.

### Table 1 General patient information

<table>
<thead>
<tr>
<th>Patient</th>
<th>General information</th>
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<tbody>
<tr>
<td>Gender and age</td>
<td>Male, 24 years old.</td>
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<tr>
<td>Immediate history</td>
<td>The patient was found in a coma after acute carbon monoxide intoxication caused by burning coal gas in a hot water heater for 1 hour, 7 days ago. On admission to a local hospital, the patient’s carbon monoxide hemoglobin was 15.4%. A diagnosis of carbon monoxide poisoning was made, and hyperbaric oxygen therapy was undertaken. Over the next 2 days, the patient became alert. In this period, he experienced generalized seizures three times, lasting for approximately 10 minutes each. He was discharged from hospital after recovery 5 days later. Two days after he was discharged, he experienced headache and visual impairment, and visited our hospital presenting with an aggravation of these symptoms.</td>
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<tr>
<td>Past history</td>
<td>Unremarkable.</td>
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<tr>
<td>Physical examination</td>
<td>Unremarkable.</td>
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<tr>
<td>Auxiliary examination</td>
<td>Blood and cerebrospinal fluid examinations revealed no abnormal findings. Visual field examination revealed right homonymous hemianopia (Figure 1). No abnormality was found on cranial MRI or magnetic resonance angiography (Figure 2). Electroencephalography displayed widespread low amplitude 8 wave activity (Figure 3).</td>
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<td>Diagnosis</td>
<td>Delayed encephalopathy after acute carbon monoxide poisoning was diagnosed, based on the following factors: (1) Definite history of acute carbon monoxide poisoning. (2) Patient had a clinical quiescent period for a few days. (3) Patient exhibited symptoms related to cortex injury. (4) Elimination of other diseases that might cause these symptoms.</td>
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<td>Treatment</td>
<td>Hyperbaric oxygen therapy was used to ameliorate the lack of oxygen to the brain&lt;sup&gt;10&lt;/sup&gt;. Also, anti-edema agents (methylprednisolone 80 mg per day) and neuro-protective agents were given. Two weeks after treatment, visual impairment was largely recovered (Figure 1).</td>
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<td>New symptoms</td>
<td>Although the patient’s visual impairment was largely recovered, he exhibited digit and letter alexia. He was able to read a newspaper in Chinese, but failed to identify the time on a clock and was unable to read single English letters shown on paper. Further assessment revealed that he was able to fluently speak some phrases and sentences in English.</td>
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<td>Evaluation</td>
<td>The Chinese aphasia battery&lt;sup&gt;10&lt;/sup&gt; and the number and letter battery supplement were conducted. (1) Aphasia battery of Chinese The patient exhibited preserved expression, comprehension, repetition, naming, and reading abilities, but difficulty in writing Chinese characters, including neologisms (Figures 4 and 5). (2) Number Count: The patient was able to count from one to ten, as well as back from ten in sequence. Repeat: The patient was able to use gestures to repeat a number smaller than ten after it was verbally presented. Reading number: Of 20 trials containing a number between 100 and 999, the patient made mistakes on 10 trials (50%). For example, “338”, “938”, “988” were read as “336”, “936” and “986”, respectively. The error rate for numbers larger than 1 000 reached 100%, accompanied by impaired identification of the digit, such as “1 034” to “18 641”. Reading formula: The patient made mistakes in reading formulae, and the following calculations. Among the following formulas, “3 + 6”, “13 + 7”, “9 × 2”, “6 × 2”, “18 + 6”, “9 + 3”, “1 + 1 = 2”, “10 - 7 = 3” were recognized as “36”, “1 x 3 + 7”, “91”, “6 x 7”, “18%6”, “9 + 1 = 3”, “1 + 1 = 1 + 27”, “21 013” respectively. Dictation: 100% accuracy. Copy: The patient was instructed to read and then copy 20 numbers. He made mistakes with all numbers larger than 100.</td>
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<td>Outcomes</td>
<td>The patient continued to receive hyperbaric oxygen therapy, as well as a low dose of methylprednisolone. After another 12 days of treatment, the patient showed a marked recovery in letter and Arabic number reading, as well as writing Chinese characters (Figures 4 and 5). Electroencephalography revealed an apparent improvement, in which an 8–9 Hz α wave returned to the typical background rhythm.</td>
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</table>
Figure 1  Visual impairment of the patient before and after treatment. Visual field examination was performed at day 2 when the patient was admitted to the hospital. Right homonymous hemianopia was evident in both eyes pre-treatment (A). After 2 weeks of treatment, the patient's visual deficit had fully recovered (B).

Figure 2  Brain imaging examination. T2-weighted brain magnetic resonance imaging (A) and magnetic resonance angiography (B) at 8 days after carbon monoxide intoxication revealed no abnormal findings. R: Right.

Figure 3  Electroencephalography at 10 days after carbon monoxide poisoning. Widespread 6.5 – 7.5 Hz slow wave activity with low amplitude could be seen. When the patient was discharged from the hospital, electroencephalography revealed apparent improvement, and 8 – 9 Hz α wave activity returned as the predominant background rhythm.

Figure 4  The patient was asked to write his name, address and occupation. Before treatment, the patient was unable to complete this task. After treatment, the patient completed the task accurately.

Figure 5  The patient was asked to copy the Chinese words shown on the left. The patient exhibited difficulty before treatment, but not after treatment.
In the current study, cranial MRI did not support the diagnosis of stroke and metabolism diseases (Figure 2). The clinical history did not provide information indicating the development of alexia, except after the carbon monoxide poisoning. Successful treatment of delayed encephalopathy after acute carbon monoxide poisoning also supported the diagnosis.

**DISCUSSION**

The symptoms of carbon monoxide poisoning are nonspecific. Delayed encephalopathy typically occurs suddenly after a lucid interval following acute exposure. Common symptoms of delayed encephalopathy include memory loss, cognitive dysfunction and neuropsychological impairment due to cerebral cortex damage, as well as pyramidal and extrapyramidal syndromes involving the globus pallidus and subcortical white matter.

In a number evaluation task, the patient was unable to read eight out of ten formulas or ten out of twenty numbers in the hundreds. In addition, he could not correctly recognize the digits of any numbers in the thousands. Most of these errors were not due to simple visual spatial impairment, which is typically exhibited as mistakenly recognizing “9” as “6”, or “13” as “31”. The present results indicated that our patient’s condition was related to an impairment of the connection between visual identification and reading of numbers. The specific brain regions underlying the patient’s impaired letter and number reading ability, but preserved Chinese character reading ability, are currently unclear. The cerebral cortex is known to be susceptible to anoxia. Previous studies have reported that damage to the cortex, globus pallidus, cerebral deep white matter, putamen, caudate nucleus, thalamus and hippocampus exhibit abnormalities that are observable on magnetic resonance imaging scans in cases of delayed encephalopathy.[13-14]. In the current study, no abnormality was observed on magnetic resonance imaging and magnetic resonance angiography scans, which eliminates the diagnosis of stroke or metabolic diseases. Electroencephalography was used to record the electrical activity of the brain. Although it may not be possible to determine the nature of the disease by the appearance of the electroencephalographic signal alone, diffuse slow wave activity in a conscious person typically indicates injury to the whole cortex in varying degrees. This measure may be more sensitive than magnetic resonance imaging. In the current patient, a partial defect in the visual field and widespread low amplitude θ wave on electroencephalography were observed, indicating neurological dysfunction of the cerebral cortex.

The cause of the patient’s letter and number alexia, but preserved Chinese character reading, remains unclear. This pattern of performance has not been previously reported, although there have been reports of selective alexia such as Hangja alexia,[15] Japanese alexia,[16] selective alexia and agraphia sparing numbers[17-18]. Some studies have suggested that the processing of ideograms and phonograms may be mediated by different brain regions. In addition, letter and number reading appear to be dependent on dissociable processes[19]. Despite the difficulties in localizing the selective alexia exhibited by our patient, we propose that focal cortical dysfunction may account for the findings of the visual field test and electroencephalography.

Functional MRI revealed activation of a wide area including left inferior/middle frontal gyri, bilateral medial frontal gyri, posterior inferior temporal area, bilateral middle occipital/fusiform gyri, and the bilateral cerebellum during Chinese letter reading[20-22]. Previous studies have indicated that Chinese characters involve more complicated neural connections compared with English letters and numbers[20]. As such, the latter may exhibit more impairment and less compensation after brain injury, because the functional brain area is relatively limited and is more likely to suffer complete damage. Recovery of writing skill is reported to be more difficult than the recovery of listening, reading or speaking[12]. This may explain why the patient’s Chinese writing ability only partially recovered after treatment, whereas his reading ability completely recovered. A less complicated and less extensive brain network is involved in the reading of numbers and letters compared with that involved in reading Chinese words[20], so less compensation may be seen after injury. This may explain why number and letter reading were more difficult to recover in the present study.

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**Author contributions:** Qingyu Shen was in charge of study concept and design, manuscript authorization. Xiaoming Rong provided data, participated in data integration and manuscript preparation. Rui Pan was responsible for data analysis. Wei Peng participated in manuscript preparation. Ying Peng was in charge of manuscript authorization. Yamei Tang was responsible for developing the study concept, manuscript preparation, manuscript authorization, and obtaining funding.
Conflicts of interest: None declared.

Ethical approval: This study was approved by the Ethics Committee, Sun Yat-sen Memorial Hospital in China.

REFERENCES


